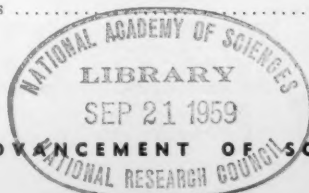


SCIENCE

18 September 1959

Volume 130, Number 3377

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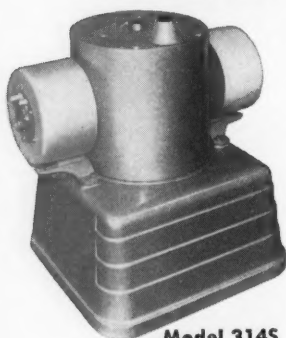
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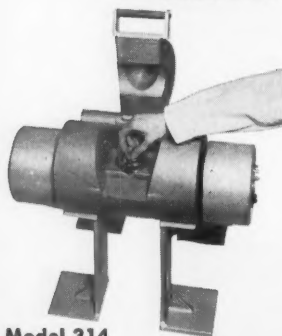
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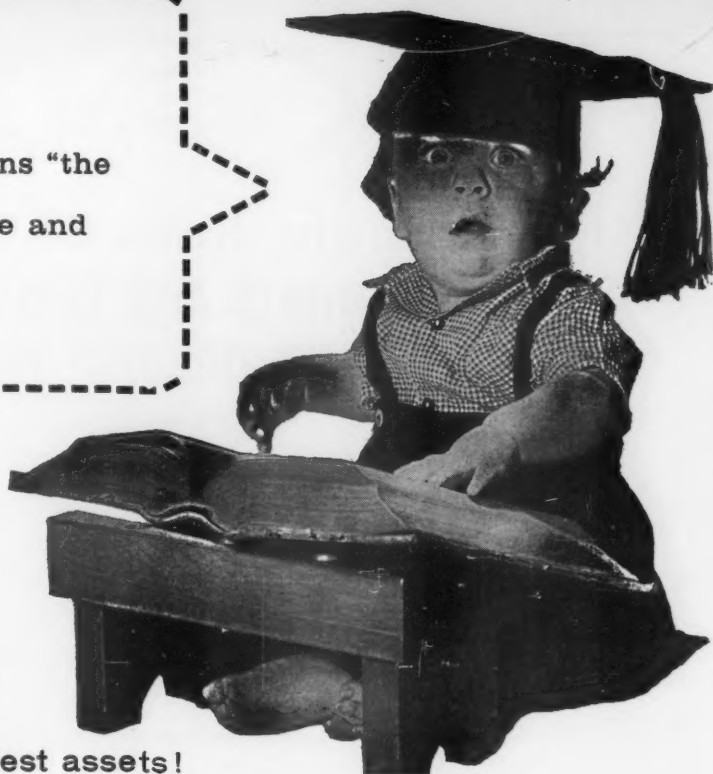
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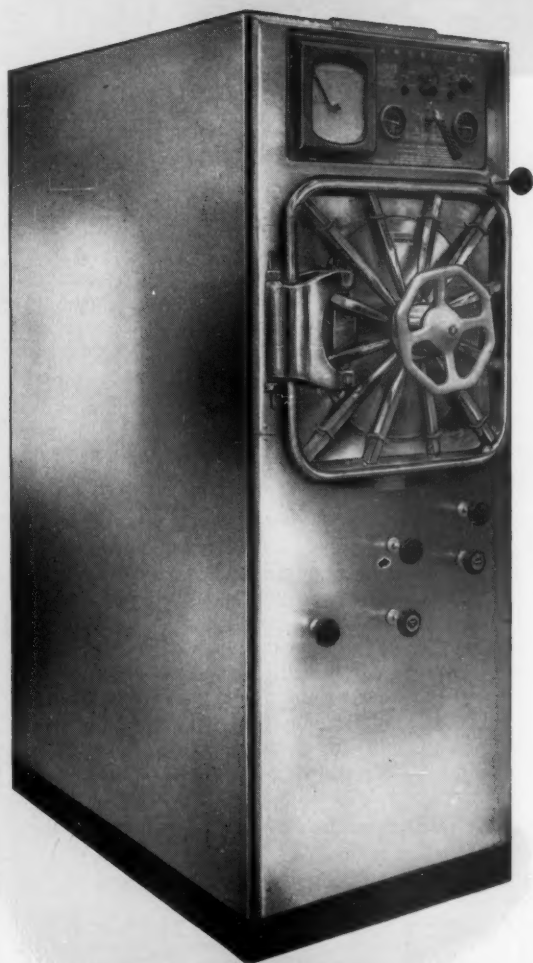
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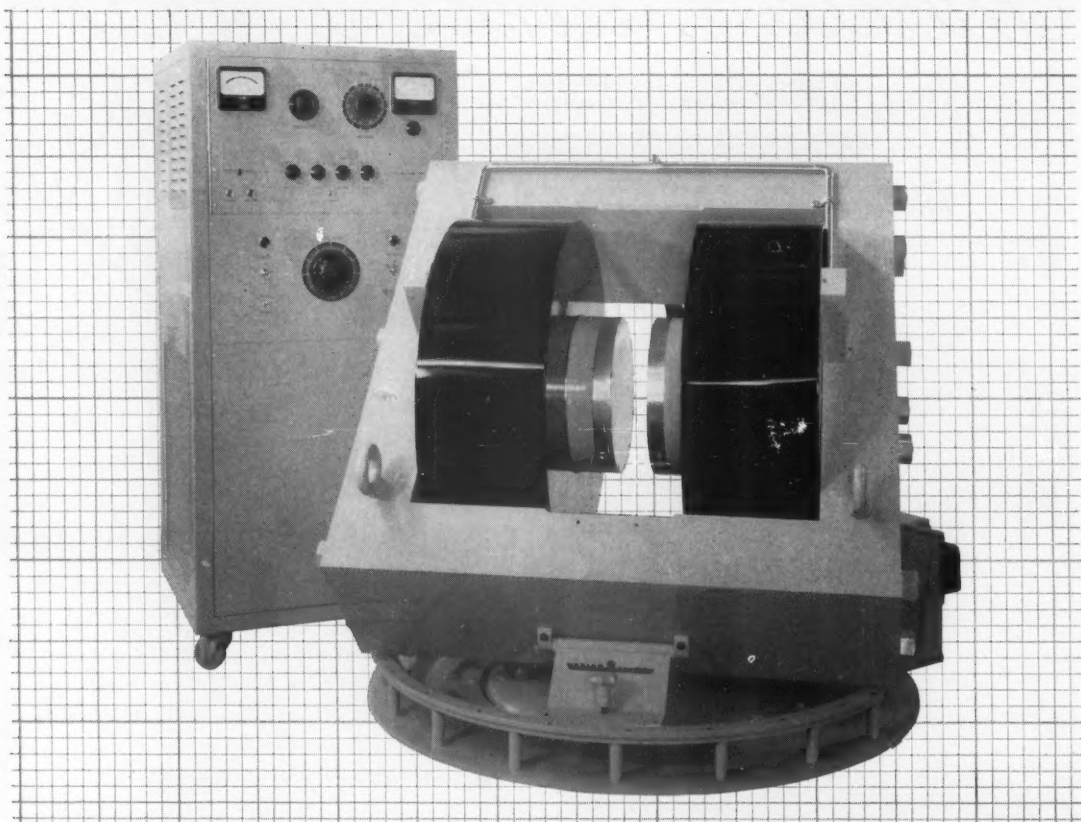
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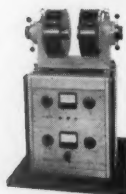
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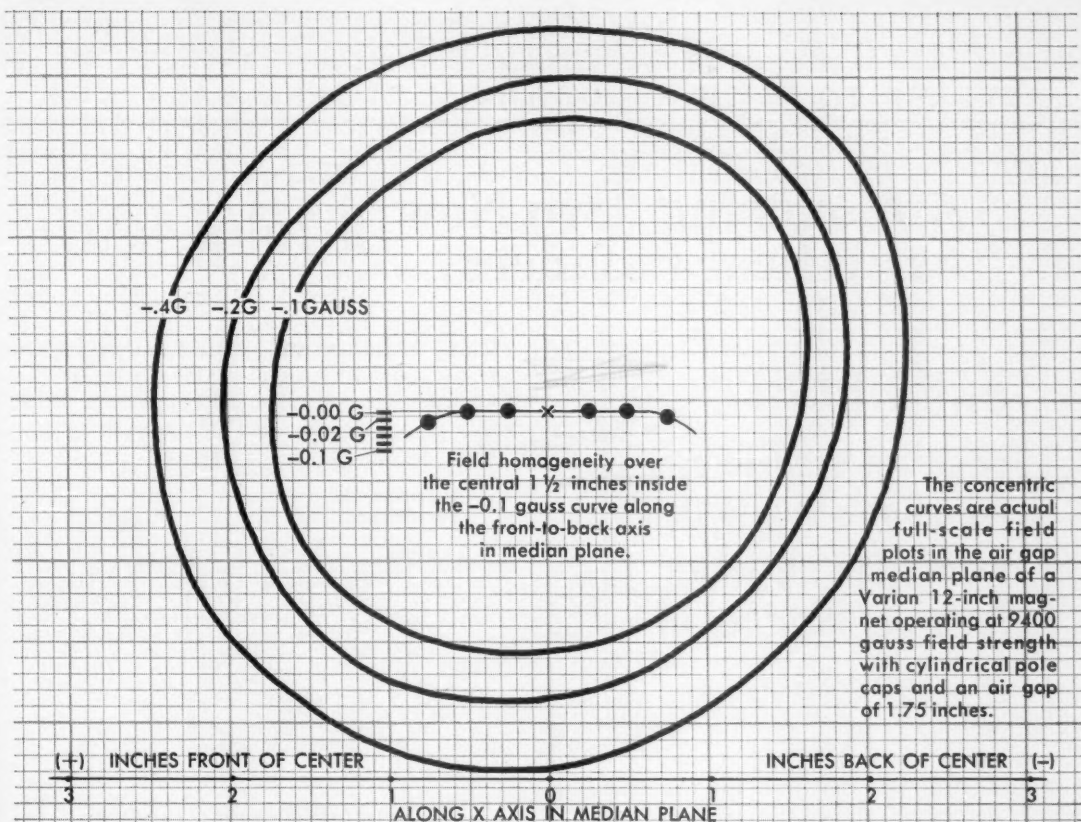
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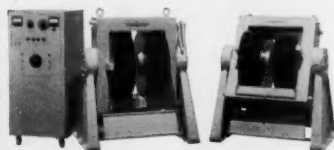
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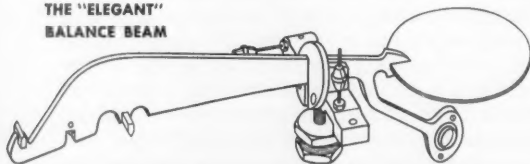


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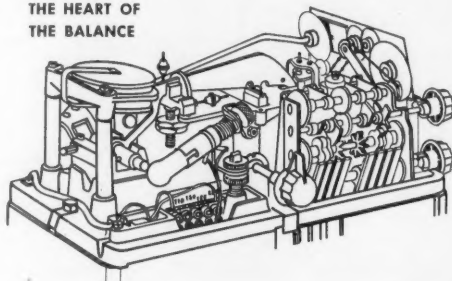
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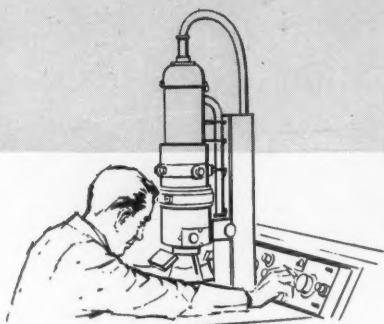
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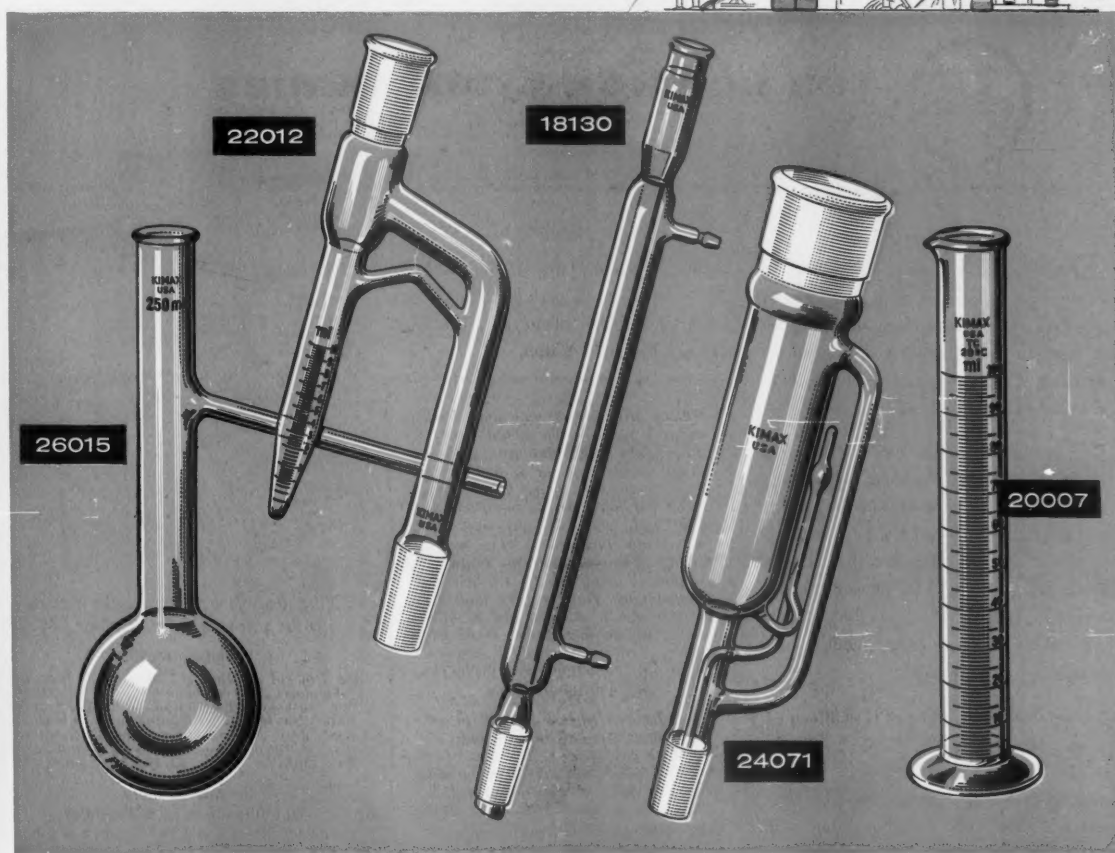
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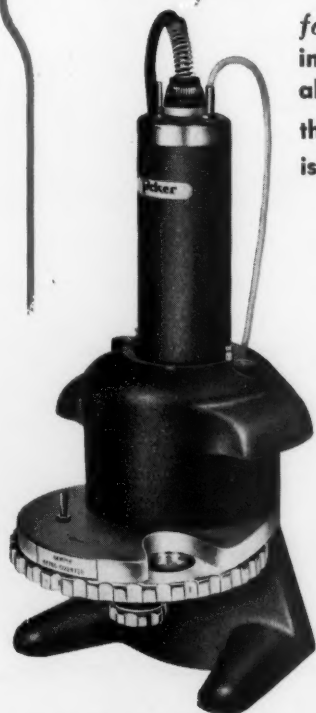
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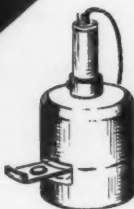
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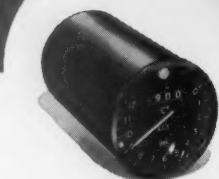
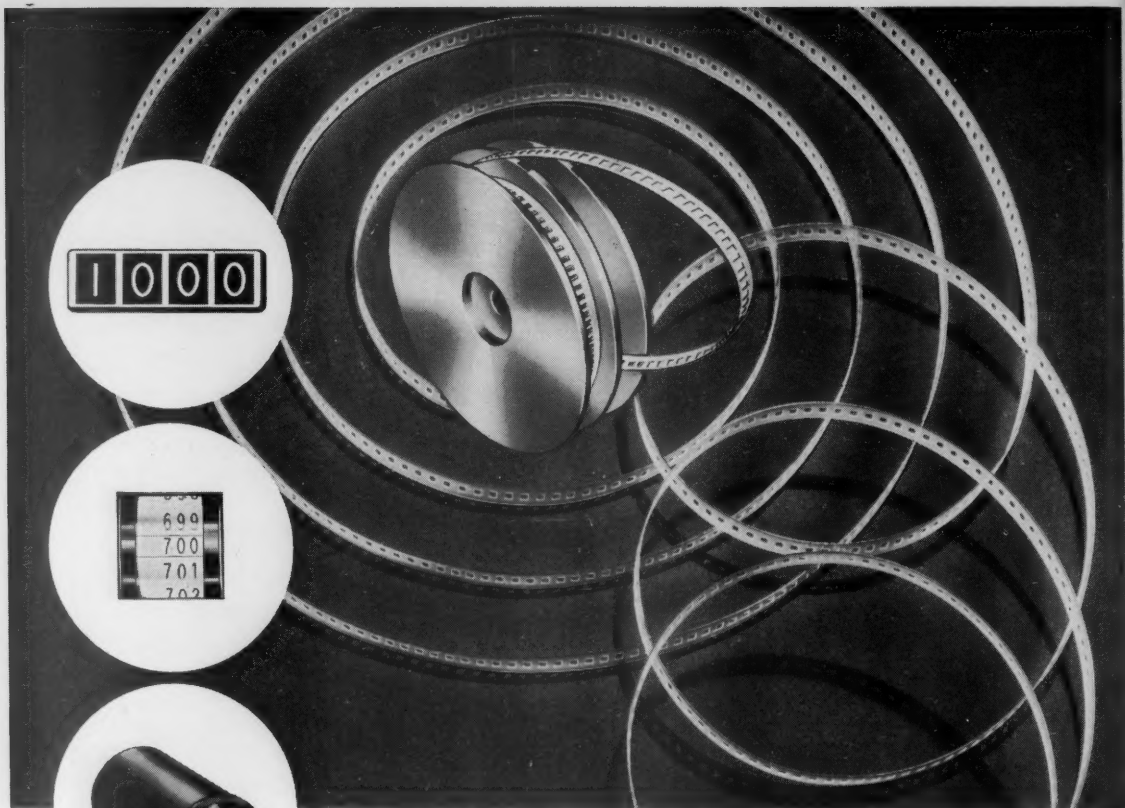
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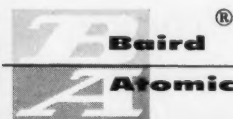
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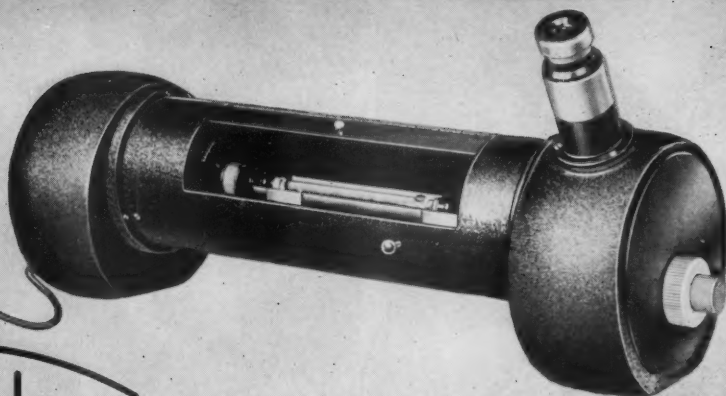


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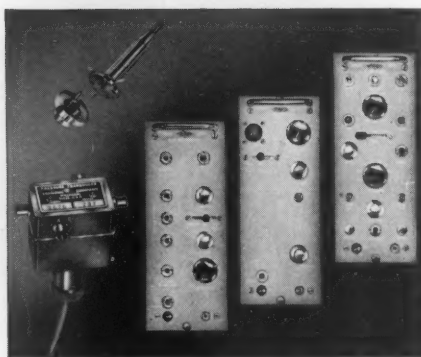
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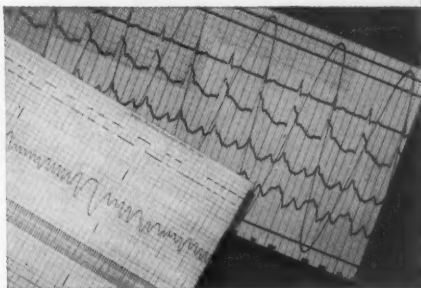
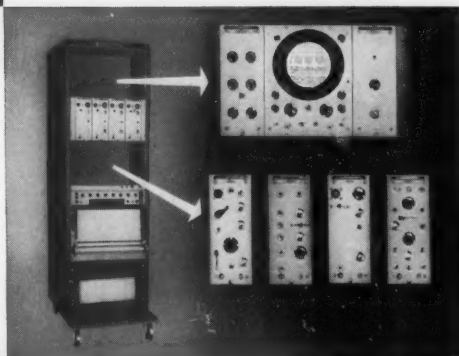


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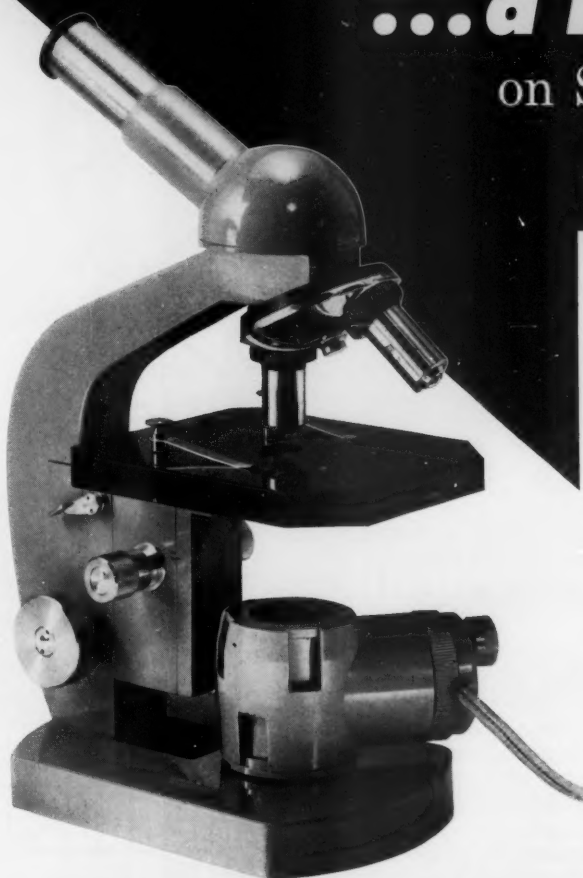


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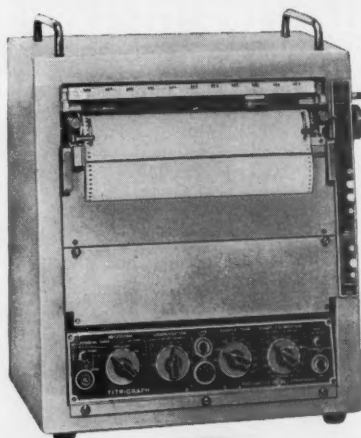
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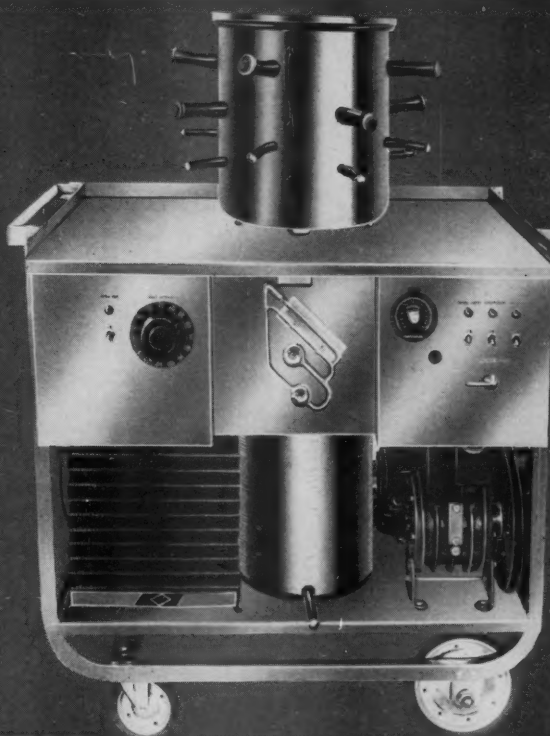
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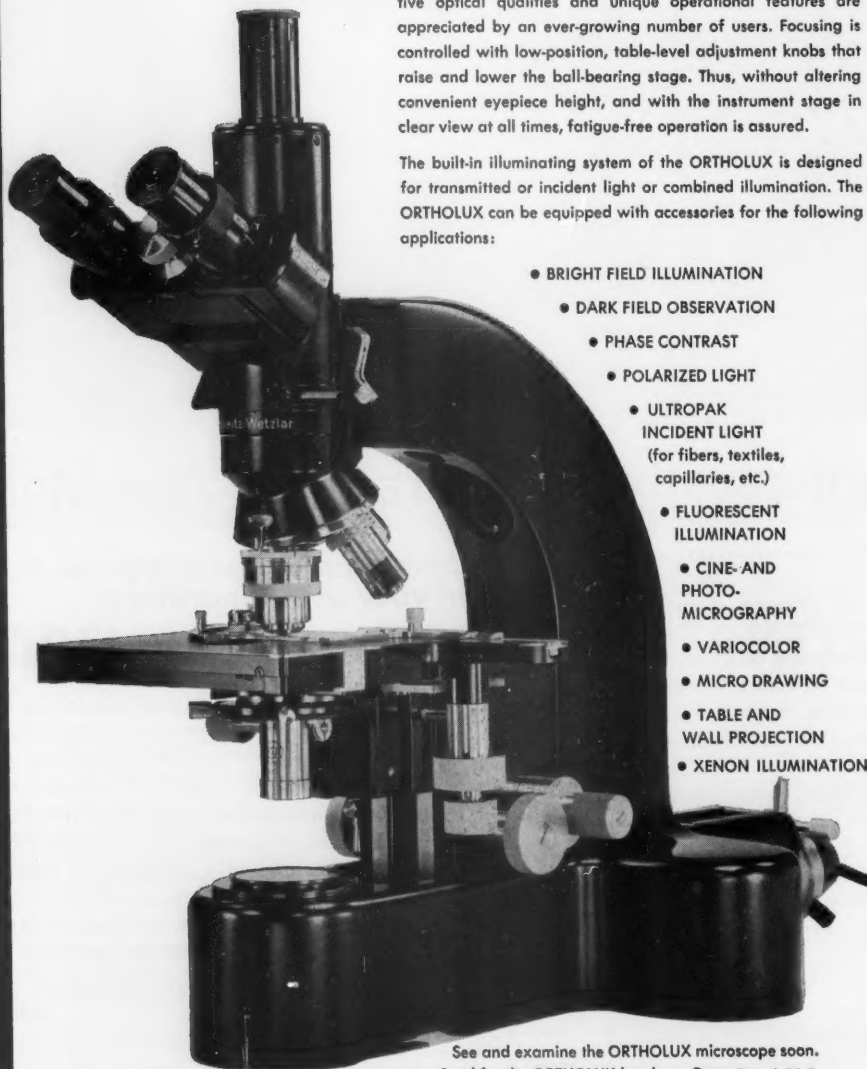
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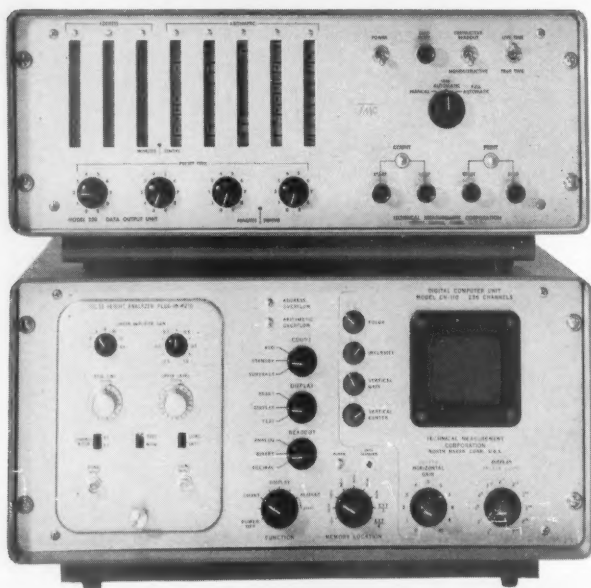
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256 THE TMC 256-CHANNEL PULSE ANALYSIS SYSTEM

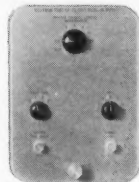


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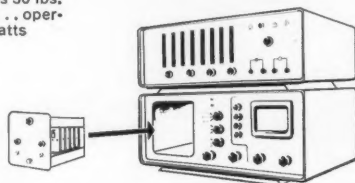
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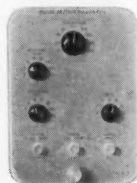


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Back to What School?

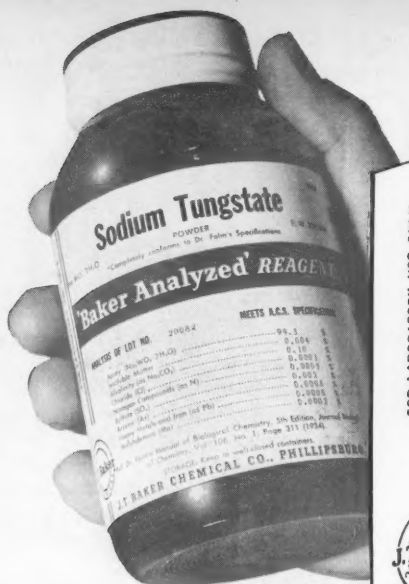
As a result in part of the recent population explosion, one person out of every four in the United States is now enrolling in school or college. Federal efforts to help the pedagogic supply meet the student demand have been estimable. Culminating in last year's National Defense Education Act, these efforts include such things as summer courses for science and mathematics teachers, purchase of laboratory equipment for schools, and loans and fellowships for college students, with special provisions for students who intend to become teachers. But despite federal assistance, the picture this year of pupils going back to, or beginning, school is not entirely inspiring.

Last month Arthur S. Flemming, Secretary of Health, Education, and Welfare, estimated that this fall we shall be short between 130,000 and 140,000 classrooms in public elementary schools and public high schools throughout the nation. How does one arrive at this figure? One way is to start with the shortage of 140,500 classrooms for fall 1958. Add the 47,400 rooms needed to meet the estimated increase in enrollments. Add the 16,800 rooms needed to replace facilities that have become unusable during the last year. And, finally, subtract the 68,440 new rooms estimated to have been built by the states. This arithmetic gives the present shortage as 136,260 classrooms. It also demonstrates that if last year's trend continues, the shortage will be solved, but only for our children's children.

To complete the picture, Commissioner of Education Lawrence G. Derthick estimated several days later that for the coming year we shall be short 190,000 qualified teachers in public and nonpublic schools. The shortage for fall 1958 was 182,000 qualified teachers. The trend again is small, but in this case we can be thankful it is small, for it is in the wrong direction. If last year's experience continues, the teacher shortage will never be solved, but at least things are going from bad to worse only gradually. Of course, newly trained teachers keep entering the profession, but the number of pupils is also growing and the dropout rate of teachers is large. According to recent figures, the dropout rate is 10.9 percent per year.

Almost everybody, including the President of the United States and a majority of the members of Congress, favors some form of federal assistance to states for school construction. However, the concerted action necessary to pass legislation is blocked by differences of opinion over how much money should be spent and how the money should be administered. Of the several major bills on the docket, the most generous is the one introduced by Senator James E. Murray and Representative Lee Metcalf, Democrats of Montana, while the most niggardly is the bill favored by the Administration. The Murray-Metcalf bill would provide federal grants of \$1.1 billion annually for four years, with the funds usable not only for new buildings but also for teachers' salaries. The Administration bill would help local school districts pay off bonds for school construction, the bonds representing a capital outlay of \$600 million. The maximum level of payments would be \$85 million per year.

Actual school needs may be greater than Secretary Flemming's and Commissioner Derthick's statistics show. Thus, estimates of the number of additional rooms needed are based on the increase in enrollments by states. But, in any one state, a large increase in enrollment in suburban areas may be offset by a decline in enrollment in nearby cities. So things may be worse, but they could also be considerably better if additional federal aid were only forthcoming.—J.T.



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CURRENT PROBLEMS IN RESEARCH

Sex Chromatin and Phenotype in Man

Disagreement between nuclear sex and phenotype raises questions about the cause of sex anomalies.

Murray L. Barr

It is now firmly established that there is a sexual dimorphism in the structure of intermitotic nuclei of man and certain other mammals. The difference between the sexes is that a special mass of chromatin or chromocenter, the sex chromatin, is clearly visible in nuclei of normal females but not in those of normal males. In normal individuals, at any rate, the presence or absence of sex chromatin is probably related to the XX sex chromosome complex of females and the XY sex chromosome complex of males.

A discrepancy between nuclear structure and the more obvious sexual features of the phenotype is found in certain developmental sex anomalies in man. For example, the phenotype is predominantly female in the Ullrich-Turner syndrome (gonadal dysgenesis), although the nuclei are usually indistinguishable from those of normal males. Similarly, the nuclei have a male structure in the syndrome of testicular feminization, but the external anatomy is strikingly feminine. Conversely, many phenotypical males with the Klinefelter syndrome (seminiferous tubule dysgenesis) have nuclei that are indistinguishable from those of normal females.

The sexual dimorphism of intermitotic nuclei has become a useful diagnostic aid, even when used empirically, in dealing with the sex anomalies (1). But the ultimate aim is an understand-

ing of the biology of the sex anomalies as a prelude to preventive measures. This requires information from the study of abnormal sex development in subhuman forms (2) and from the study of human chromosomes in dividing cells, through recently developed techniques (3, 4). This article represents an attempt to summarize current concepts of the pathogenesis of some syndromes encountered in clinical medicine, and to point out the many gaps in our knowledge that have to be filled before etiological factors can be fully understood.

Normal Gonadal Differentiation

Gonadal ridges appear in the human embryo at about the fourth week of gestation. Their structure is identical in male and female embryos until the seventh week (Fig. 1, A). The cellular cortex of the indifferent gonad has the potentiality of developing into an ovary. The medulla, consisting of primary sex cords in a mesenchymal stroma, has the potentiality of developing into a testis (5). Primordial germ cells can be identified in cortex and primary sex cords from the sixth week onward, having migrated into the gonad from the region of the extra-embryonal entoderm.

The fate of the indifferent gonad is established by the balance between male-determiners and female-determiners in the genotype (6). When the sex

chromosome complex is XY, male-determining genes on autosomes predominate over female-determining genes on the single X chromosome. The medulla begins to develop, and the cortex to regress, at the seventh week. The primary sex cords become seminiferous tubules, and interstitial cells appear between them, while the cortex becomes the thin visceral layer of the *tunica vaginalis* that adheres to the *tunica albuginea* (Fig. 1, B). It is noteworthy that the endocrine component of the testis, consisting of interstitial or Leydig cells, is well developed in the embryonal testis and again after puberty but is inconspicuous in the intervening period.

When the sex chromosome complex is XX, female-determiners on the two X chromosomes outweigh male-determiners on autosomes (7). Beginning at the ninth week, the cortex develops into an ovary through the ingrowth of secondary sex cords, and the medulla regresses (Fig. 1, C). Interference with this crucial step of differentiation of bipotential gonads into testes or ovaries, at about the end of the second month of embryonic development, appears to be the point of departure for most sex anomalies in man. The genetic balance between male-determiners and female-determiners may be altered by a mutant gene or by an abnormality of one or more of the chromosomes that bear these determiners. But experimental evidence testifies to the frequent adverse effects of various nongenetic factors on gonadal differentiation. Evidence for possible genetic or nongenetic factors that might interfere with normal gonadal differentiation has to be sought for each type of sex anomaly.

Normal Differentiation of Internal and External Genitalia

Wolffian ducts (primordia of epididymides, *vasa deferentia*, and seminal vesicles) and Müllerian ducts (primordia of Fallopian tubes, uterus, and vagina) are both present when gonadal differentiation begins, and the external genitalia are also in a bipotential state. Much experimental work bears on the factors responsible for development of internal and

The author is head of the department of microscopic anatomy, Medical School, University of Western Ontario, London, Canada.

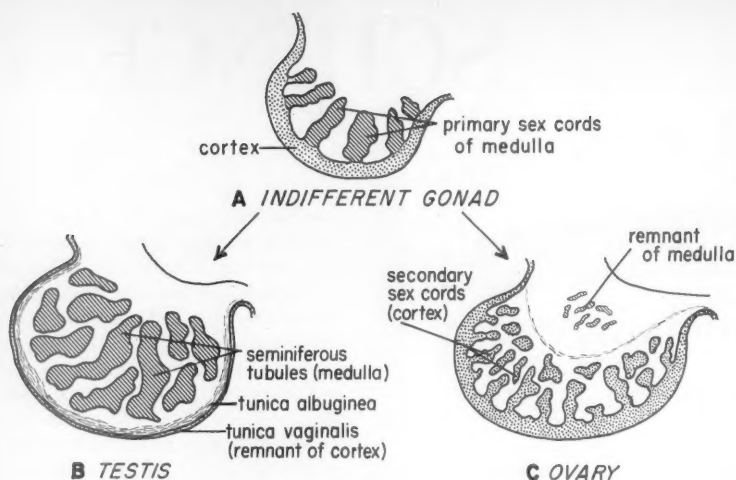


Fig. 1. Diagrammatic representation of development of a testis from the medullary component, and an ovary from the cortical component, of the indifferent gonad of an early embryo. [Modified from Grumbach and Barr, *Recent Progr. in Hormone Research* (26), courtesy Academic Press, New York]

external genitalia in a direction which is consistent with the male or female character of the gonads. Treating embryos with androgens or estrogens, transplanting an embryonal gonad into an embryo of the opposite sex, and depriving an embryo of the influence of embryonal gonads have all yielded pertinent results. The consequences of surgical removal of gonads in rabbit and rat embryos and the destruction of gonads by x-rays in mouse embryos form the basis of current hypotheses concerning the pathogenesis of sex anomalies in man (8-10). The outstanding work of Jost on rabbit embryos illustrates the results obtained in such experiments (Fig. 2).

Gonadal differentiation into testes or ovaries begins on the 15th day in the rabbit, while differentiation of the duct system begins on the 20th day and is virtually complete by the 28th day, which is about two days before birth (Fig. 2, A-B and A-D). Gonadectomy of female embryos at any stage or of male embryos at about the 20th day is followed by maturation of the duct system and the external genitalia in a female direction, although the uterus is rather smaller than normal (Fig. 2, A-C). There is normal maturation of the male genitalia if removal of the testes is delayed beyond the 24th day. These observations indicate that ovaries are not essential for female development, but that the action of an inductor or evocator from the interstitial cells of the embryonal testes is necessary during a critical period for male development. Although much

remains to be learned of the factors controlling embryogenesis of the reproductive system, the requirement of a masculinizing evocator of testicular origin to counteract a tendency of all embryos to feminize is a keystone in current concepts of the pathogenesis of congenital errors of sex development.

The masculinizing evocator appears to have a local action on adjacent tissues, since a unilateral graft of embryonal testis into a female embryo stimulates the Wolffian duct and suppresses the Müllerian duct on the side of the transplant preferentially (9, 10) (Fig.

3). A similar asymmetry follows unilateral gonadectomy of male embryos between the 20th and 24th day and occurs in human true hermaphrodites when there is testicular tissue on one side only. The substance seems to act in the manner of embryonal evocators generally, which is consistent with experimental evidence that the evocator substance differs in its physiological effects, and probably in chemical composition, from testosterone and other androgenic hormones.

The Müllerian ducts of rat embryos in the early undifferentiated stage persist and grow in vitro, and the Wolffian ducts regress, regardless of the sex of the donor (9, 10). This suggests that the inherent tendency of embryos to feminize is genetically controlled, rather than the result of an exogenous factor such as maternal estrogens. There is little information relating to genetic mechanisms that may operate in this connection. The genes involved must be other than the male-determiners and female-determiners whose balance controls gonadal differentiation, since female differentiation can occur whether the sex-chromosome complex is XX or XY.

Sexual Dimorphism of Interstitial Nuclei

Chromosomal, gonadal, and phenotypical sex are normally in agreement. But the sex-chromosome complement may be inconsistent with the main fea-

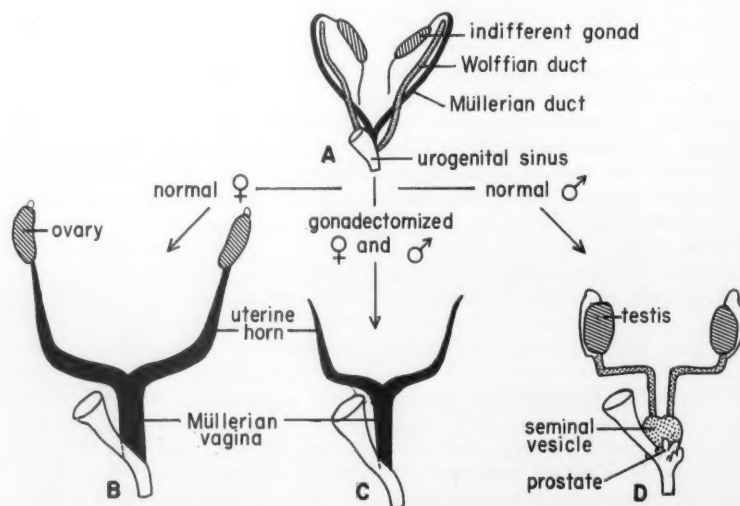


Fig. 2. Schematic representation of development of sex ducts in normal and gonadectomized rabbit embryos. [After Jost, "Sex Differentiation and Development" (51), courtesy Cambridge Univ. Press, London]

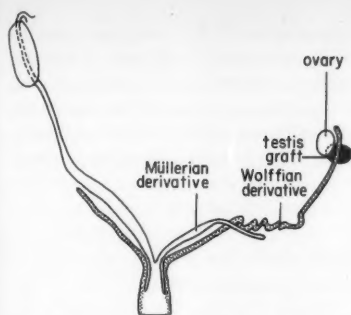


Fig. 3. Genital tract of a 28-day-old female rabbit embryo in which a testicular graft from a 21-day-old embryo had been implanted adjacent to an ovary on the 20th day of development. [After Jost, *Arch. anat. microscop. morphol. expil.* (9), courtesy Masson, Paris]

tures of the phenotype when there has been an error in gonadal differentiation. Consequently, the "tests of chromosomal sex," having as their basis a sexual dimorphism in the structure of intermitotic nuclei, are useful diagnostic aids in clinical practice and raise new problems in connection with the etiology of sex anomalies.

The sex chromatin that characterizes nuclei of females is usually adherent to the inner surface of the nuclear membrane and is often so closely related to the membrane as to have a planoconvex outline (Fig. 4, a and b) (11). It is about 1 micron in diameter and can be resolved frequently into two components of equal size. The sex chromatin shares with the rest of the chromatin an affinity for basic dyes and, like the rest of the chromatin, reacts positively to tests for deoxyribonucleic acid, staining readily with the Feulgen technique and with methyl green. In particularly favorable circumstances, as in the study of whole mounts of thin membranes, the sex chromatin can be identified in virtually every nucleus. In sections of tissues 5 microns in thickness, sex chromatin can be identified in 60 to 80 percent of the nuclei, depending on the technical quality of the preparations and such factors as the size of the nuclei and the coarseness of the general chromatin particles. A chromatin mass larger than other chromatin particles of the nucleus is encountered in up to 10 percent of the cells in sections of tissues from males. This particular mass of chromatin is seldom as large as the sex chromatin of females, and its significance is uncertain.

Neutrophils have a different kind of sexual dimorphism (Fig. 4, c) (12). In a small proportion of neutrophils of fe-

males (1 to 10 percent, average about 3 percent), there is an accessory nuclear lobule; such a lobule is encountered with the greatest rarity, if at all, in neutrophils of males. The relation of the accessory nuclear lobule to the sex chromatin is not known.

Nuclei have been examined for sex chromatin in 24 mammalian representatives, more extensively in some than in others (Table 1) (13). In man and monkey, the imprint of sex on nuclear structure is present in the various tissues and organs, cells with small pyknotic nuclei excepted. This is also true of those carnivores that have been studied extensively and probably holds for carnivores generally. Nerve-cell nuclei bear a clear imprint of sex in the few representatives of the order Artiodactyla that have been studied, but the nuclear chromatin is too coarse in nonnervous tissues to allow identification of the sex. In the Virginia opossum, the only marsupial that has been examined, sex chromatin is present in nuclei of both sexes, but the size is significantly larger in females. There are multiple large particles of chromatin in nuclei of the rabbit and of rodents, so these animals are unsuitable for work that depends on the sex characteristics of intermitotic nuclei. But there are exceptions, for the sex chromatin can be identified in motor neurons of female rats and hamsters and in ameloblasts of newborn rats, and the sex-identifying variant that occurs in neutrophils of man is also present in those of the rabbit. Representatives of an order appear to have similar nuclear characteristics with respect to the coarseness of the chromatin particles and the clarity of the sex chromatin of females.

Nuclear dimorphism according to sex is lacking in the very early stages of embryonic development. In the cat, for example, this feature could not be detected in the morula stage and was seldom seen in blastocysts. Neither has sex chromatin been described in ova of pri-

Table 1. Sexual dimorphism in cell nuclei of mammals.

Representatives	Dimorphism present?
<i>Primates</i>	
Man	Yes
Monkey	Yes
<i>Carnivora</i>	
Cat	Yes
Dog	Yes
Mink	Yes
Marten	Yes
Ferret	Yes
Raccoon	Yes
Skunk	Yes
Coyote	Yes
Wolf	Yes
Bear	Yes
Fox	Yes
<i>Artiodactyla</i>	
Goat	Yes
Deer	Yes
Swine	Yes
Cattle	Yes
<i>Marsupialia</i>	
Opossum	Yes
<i>Lagomorpha</i>	
Rabbit	No
<i>Rodentia</i>	
Rat	No
Hamster	No
Mouse	No
Guinea pig	No
Ground hog	No

mary follicles. But nuclear dimorphism is clearly established in embryos of the cat well before gonadal differentiation, and the imprint of sex is visible in resting nuclei of human and macaque embryos from the 12th to the 19th day onward (14).

Since the sex chromatin is a Feulgen-positive chromocenter, it presumably represents positively heterochromatic regions of chromosomes—that is, regions that are dense and prominent when the euchromatic regions are indistinct. The fine details of the sex chromatin, especially its bipartite structure and its connection with a delicate thread that may also be double, as well as the multiple masses of sex chromatin that are present



Fig. 4. Nuclei of human females. (a) Nuclei in epidermis of a skin biopsy specimen (hematoxylin-eosin); (b) nucleus in an oral mucosal smear (cresylecht violet); (c) neutrophil in a blood film (Giemsa). (\times about 1680.) [After Barr, *Brit. J. Urol.* (52), courtesy Livingstone, Edinburgh]

in polyploid nuclei, suggest that it is formed from heterochromatic regions of a pair of homologous chromosomes (15). Although an alternative interpretation has been suggested (16), the weight of evidence favors the view that the bipartite sex chromatin of females is formed by heterochromatic regions of the two X chromosomes, and that a definite chromocenter is not formed by the nonhomologous sex chromosomes of the heterogametic sex (17). This interpretation implies somatic pairing, for the X chromosomes at any rate (18). Somatic association of heterochromatic X chromosomes has, indeed, been described in ovarian follicular cells of the mouse (19).

The sex chromosomes vary in their heterochromaticity in different cell types, depending, possibly, on differences in the immediate environment of the chromosomes. As mentioned above, sex chromatin has not been described in ova and is lacking in the very early stages of embryonic development, while the XX complex forms a definite chromocenter throughout the rest of the life span of females. Conversely, the XY complex is strongly heterochromatic in prophase of meiosis but seldom produces a recognizable chromocenter in somatic cells. Other variants are on record. For example, the X and Y chromosomes form separate chromocenters of the same size in somatic cells of the ground vole, so that nuclei of males and females cannot be distinguished from each other; the multiple X chromosomes of certain insects form individual chromocenters, the sexes being divergent with respect to the number of these chromocenters that are formed; and the XY, rather than the XX, complex forms a distinctive chromocenter in somatic cells of the silkworm and the spruce budworm, in which the female is the heterogametic sex (20, 21).

Tests of Chromosomal Sex in Clinical Medicine

Application of the principle of nuclear sexual dimorphism to the study of patients with sex anomalies requires only an easily obtainable source of cells (12, 22). A skin biopsy specimen may be studied, since the sex characteristics of the nuclei are well defined in the mature spinous cells of the epidermis and in the large spherical nuclei of hair follicles (Fig. 4, a). A smear preparation of oral epithelium is particularly easy to obtain

and is the favored procedure on that account (Fig. 4, b). Although whole nuclei are present in oral smears, the incidence of nuclei with unequivocal sex chromatin is low (30 to 60 percent) in chromosomal females, and in an occasional preparation the sex chromatin is less conspicuous than usual because of being much flattened against the nuclear membrane. However, these factors do not seriously lessen the usefulness of the oral-smear method, because chromocenters at the nuclear membrane that could be interpreted as sex chromatin occur with the greatest rarity in smears from chromosomal males. The neutrophil method (Fig. 4, c) gives the same information as is derived from the more conventional skin-biopsy and oral-smear techniques. Preparations of high technical quality are required for each of the tests. The preferred technical procedures are given elsewhere (23).

A correlation between the presence of sex chromatin and XX sex chromosomes, or the absence of sex chromatin and XY sex chromosomes, can logically be assumed for normal individuals. But the interpretation is not necessarily so straightforward in the sex anomalies (24). The possibility of a chromosomal abnormality need not be considered when the congenital error clearly does not involve the genetic sex-determiners. For example, the sex chromatin indicates the XX complex in the adrenogenital syndrome, where the fetal adrenal cortex is at fault, and when there is partial masculinization of the external genitalia in a female newborn whose mother received progestins during pregnancy (25). In addition, a chromosomal abnormality, other than sex chromosomes that are inconsistent with the phenotype, need not be suspected if the congenital error can be clearly attributed to a mutant gene or genes among the sex-determiners.

If the foregoing conditions are not fulfilled, the presence of sex chromatin in the "tests of chromosomal sex" means only that the nuclei contain heterochromatic regions of two X chromosomes. One of these chromosomes may be defective in its euchromatic region, there may be an unusual sex chromosome complex (such as XXY), or the autosomes that bear male-determiners may be in some way abnormal. Conversely, absence of sex chromatin in the "tests of chromosomal sex" indicates that two normal X chromosomes are not present. The sex chromosome constitution could, in theory, be XO, or there could be an

abnormality of the autosomes carrying male-determiners. Awareness of the possibility of chromosomal abnormalities as a basis for some genetic sex anomalies should stimulate study of whole-chromosome complements by techniques that are now available.

Congenital Errors of Sex Development in Man

The hermaphrodite group was the main center of interest until recently. Hermaphrodites were known in ancient times and have always attracted attention because of the bizarre intersexual morphology of the external genitalia. There are three main varieties. Both testicular and ovarian tissues are present in *true hermaphrodites*. The nuclei have a female chromatin pattern in some patients and a male chromatin pattern in others. *Male pseudohermaphrodites* have testes, and the nuclei are always male. The internal and external genitalia have an intersexual morphology in true hermaphrodites and male pseudohermaphrodites, but the details vary widely from one subject to another. Through some physiological deficiency, the evocator produced by the embryonal testes has failed to bring about full masculinization of the reproductive system in the male pseudohermaphrodite.

Female pseudohermaphrodites have ovaries and essentially normal female internal genitalia. But there is persistence of the fetal urogenital sinus, clitoral hypertrophy, and at times partial fusion of the labioscrotal folds to produce intersexual external genitalia. With few exceptions, the condition is the result of hyperplasia of the fetal adrenal cortex and elaboration of androgenic steroids in excessive amounts. The sex chromosome complement is always XX. The hermaphrodite group is described in detail in the classical book by Young, and the discussion is bought up to date in recent publications (16, 26, 27). The following account is limited to errors of sex development in which there is an extreme divergence between the phenotype and the nuclear chromatin pattern.

Gonadal Dysgenesis

Gonadal dysgenesis (or virtual agenesis) is encountered as a component of the Ullrich-Turner syndrome. The individual has a female phenotype, with essentially normal external genitalia,

vagina, uterus, and tubes. The principal defect is in the gonads, which are represented by slender streaks of connective tissue, simulating ovarian stroma, attached to the broad ligaments (Fig. 5). Derivatives of mesonephric ducts may be present, but there is rarely any evidence of ovarian follicles or seminiferous tubules in the typical syndrome, except possibly during the neonatal period (28). Various congenital abnormalities are associated with gonadal dysgenesis. Shortness of stature is almost the rule, and there are often cutaneous folds at the sides of the neck. Less frequently, there may be a variety of skeletal or vascular anomalies and a number of other defects. Urinary excretion of pituitary gonadotropins is elevated after the age of 10 years, and secondary sex characteristics fail to develop naturally at puberty.

Both Jost and Wilkins suggested that a proportion of individuals with gonadal dysgenesis might be chromosomal males, the embryos having feminized in the absence of the masculinizing evocator of testicular origin (9, 10, 29). This prediction was verified promptly (30) when tests of chromosomal sex became available, at least to the extent that 80 percent of subjects with gonadal dysgenesis are now known to have a male chromatin pattern, while the remainder have a female chromatin pattern (31, 32).

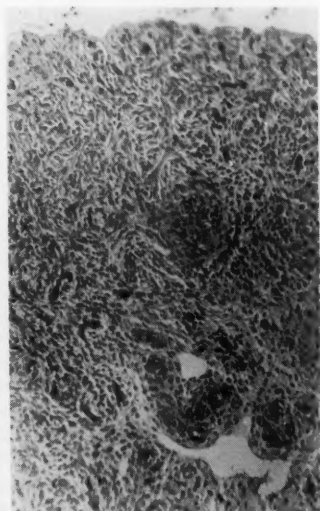
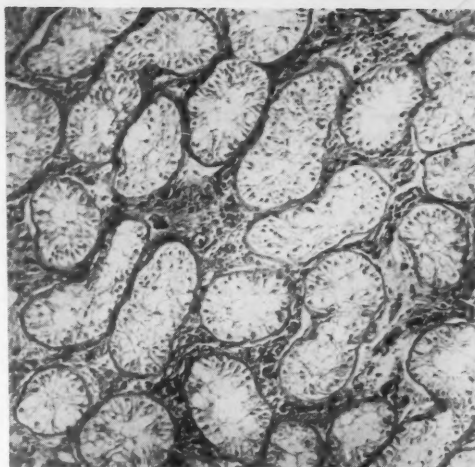


Fig. 5. Gonad consisting entirely of connective tissue that simulates ovarian stroma, in a 4-year-old girl with gonadal dysgenesis and a male chromatin pattern. (Hematoxylin-eosin.) ($\times 125$) [Courtesy Melvin M. Grumbach]

Fig. 6. Testis from a subject with the syndrome of testicular feminization. There are adequate Leydig cells, but the seminiferous tubules show the inhibition of spermatogenesis that occurs in undescended testes. (Hematoxylin-eosin.) ($\times 85$)



But the etiological factor responsible for failure of gonadal development and for the associated anomalies remains obscure. A maternal factor is a possibility, although none has yet been demonstrated (28, 31). Or an adverse nongenetic factor may originate in the zygote, following, for example, the fertilization of an overripe ovum (33). If the etiology of the Ullrich-Turner syndrome proves to be nongenetic or if a mutant gene with pleiotropic manifestations is responsible, the sex chromosome complement would be XY or XX, in accordance with the structure of the intermitotic nuclei. Tests of color vision indicate that those with sex chromatin bear the XX complex and that those without sex chromatin bear the XY (or XO) sex chromosome complex (34). Other methods of study, especially the examination of entire chromosome complements at metaphase, are needed to investigate the possibility of chromosomal anomalies that would not be visible in intermitotic nuclei (21, 35).

Whatever the etiology of the virtual agenesis of the gonads proves to be, embryological development proceeds along female lines in accordance with the principle that an evocator of testicular origin is required for masculinization.

Testicular Feminization

The syndrome of feminizing testes is another condition in which the phenotype is predominantly female, although the intermitotic nuclei have a male chromatin pattern and probably contain the XY sex chromosome complex (26, 36). The syndrome is in some respects an extreme form of male pseudoher-

maphroditism, but there are unique features that justify its consideration as a distinct entity.

The external genitalia are normally female in the typical syndrome, but pubic hair is often lacking. The vagina is a blind pouch, uterus and tubes being usually absent. Testes are present bilaterally in the pelvis or inguinal regions, accompanied by epididymides and proximal portions of *vasa deferentia*. The seminiferous tubules are immature (Fig. 6) because of the undescended position of the testes. Leydig cells are present in normal numbers. There is a normal female habitus, and the breasts develop well at puberty. The secondary sex characteristics are, in fact, strikingly feminine, and primary amenorrhoea may be the only overt indication of an abnormality of the reproductive system.

The syndrome is a hereditary anomaly that is transmitted by normal mothers. In families that include these subjects, there is a normal sex ratio if those with testicular feminization are added to normal males. The anomaly is probably caused by a mutant gene, but examination of the chromosome complement at metaphase is required to rule out a chromosomal abnormality consistent with male-type intermitotic nuclei. A quantitative or qualitative defect in the production of the evocator by interstitial cells is probably responsible for failure of male development in those parts of the reproductive system that are farthest from the testes. The interstitial cells clearly have a perverse metabolism, as shown by the development of feminine secondary sex characteristics at puberty and by the onset of menopausal symptoms if the testes are removed.

Seminiferous Tubule Dysgenesis (Klinefelter's Syndrome)

The Klinefelter syndrome includes subjects in whom there is a discrepancy between the phenotype and nuclear structure which is the reverse of that found in most individuals with gonadal agenesis and in those with the syndrome of feminizing testes.

The reproductive system has undergone normal male development, except that the testes are small and sperms are lacking from the semen. Eunuchoid traits may be present, and there is gynecomastia occasionally. Increased urinary excretion of pituitary gonadotropins is almost the rule, and the level of urinary 17-ketosteroids may be decreased (37). There was no reason to suspect a discrepancy between nuclear structure and the phenotype in any of these subjects, and the discrepancy was noted in the routine application of tests of chromosomal sex to various types of disorder of the reproductive system (38). The proportion of subjects who satisfy the clinical requirements for inclusion in the syndrome and who have a female chromatin pattern is not known exactly; three out of four may be a reasonable assumption.

The unusual histological structure of the testes is the most significant finding, and it differs to some extent, depending on whether the nuclei are female or male. The seminiferous tubules are highly abnormal when the nuclei are female. They are commonly represented by hyaline masses (Fig. 7, *a*), or there may be small tubules, with a thickened *lamina propria*, that contain Sertoli cells or epithelial-like cells of a type difficult to identify (Fig. 7, *b*). Spermatogonia or even more mature germ cells are present in a few tubules of some individuals. Spermatogenesis to the stage of mature sperms is encountered only rarely but is compatible with a female chromatin pattern in the somatic cells. The appearance of Leydig cells in large clumps contrasts with their scattered arrangement in normal testes. When the nuclei are male, the tubular defects are less severe and the Leydig cells are in smaller aggregates.

The results of family studies suggest a genetic etiology of the Klinefelter syndrome (39). If a mutant gene among the sex-determiners is responsible, the sex-chromosome complex would be XX or XY according to the chromatin pattern. Tests of color vision have yielded conflicting results (40). However, there may be an XXY complex or a deficiency

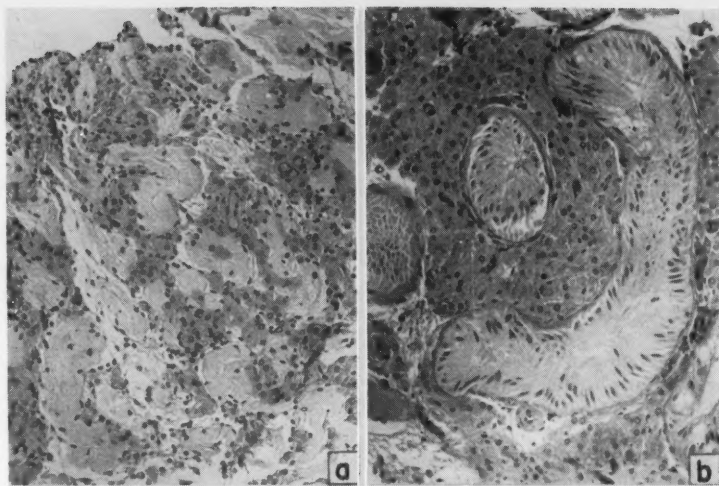


Fig. 7. Photomicrographs illustrating gonadal structure in seminiferous tubule dysgenesis (Klinefelter's syndrome) in a subject with a female chromatin pattern. The tubules may be reduced to hyalinized masses (*a*), or they may have thickened fibrous tunics and grossly defective epithelia (*b*). The Leydig cells are in large aggregates. Hematoxylin-eosin. ($\times 125$)

in the euchromatic portion of an X chromosome when the nuclei are female, or there may be an abnormality of the autosomes that bear male-determiners whether the nuclei are female or male. In this condition, probably even more than in the other sex anomalies, it will be necessary to study the entire chromosome complement in metaphase. A beginning in this direction has been made (4, 41).

Whatever the precise etiological factor may be, testis-like gonads develop from the indifferent gonads of the early embryo regardless of whether the nuclei have female or male characteristics. Although there is severe dysgenesis of the seminiferous tubules, the abundant interstitial cells produce the evocator that masculinizes the embryo, resulting in an individual who has a male phenotype. A full understanding of the syndrome of seminiferous tubule dysgenesis is particularly desirable because of its association, in many instances, with some degree of mental retardation (42).

Concluding Remarks

The principle of sexual dimorphism in the structure of intermitotic nuclei is well established and forms the basis of the "tests of chromosomal sex" that are valuable adjuncts to diagnosis in clinical medicine. An attempt has been made to point out deficiencies in our knowledge that may attract the attention and interest of biologists. The etiol-

ogy of the sex anomalies is in need of clarification, and a study of entire chromosome complements would be especially helpful. Other lines of investigation are suggested by the problems discussed during the Symposium on Nuclear Sex that was held in London, England, in September 1957 (43).

Addendum

Several reports that have an intimate bearing on this subject appeared after submission of the manuscript.

At the time of preparation of the paper, there were two reports that dealt with the sex chromosome complex in a sex anomaly, as determined by the new cytological techniques, but they were in disagreement (4, 41). Ford *et al.* (44) have now described an XX/XXY mosaicism in a patient with the Klinefelter syndrome and a female chromatin pattern, which approaches the description of an XXY complex in a similar patient by Jacobs and Strong (41). I understand that the presence of an XXY complex in such subjects has been confirmed by unpublished work in several laboratories. On the basis of this finding, Stern (45) was able to resolve the seemingly divergent results that had been recorded in connection with tests of color vision in patients with the Klinefelter syndrome (40).

The presence of an extra chromosome, which is one of the smallest autosomes, has been demonstrated in mongolism

(46). A somatic cell chromosome number of 48, rather than the normal 46, has been found in a unique individual with both mongolism and the Klinefelter syndrome (47). One of the extra chromosomes was the small autosome that occurs in mongolism; the other was contributed by the unusual XXY sex chromosome complex of the Klinefelter syndrome. Important observations are also being made on the sex chromosome complement in cases of gonadal dysgenesis or Turner's syndrome, in which a single X chromosome, unpaired with either another X chromosome or a Y chromosome, has been described (48).

These observations necessitate a revision of the currently accepted hypothesis of genetic sex-determining mechanisms in man, which are based on cytogenetic studies in *Drosophila*. It now appears that the Y chromosome, far from having a passive role in sex determination, contains potent male-determining genes. In fact, the gonads have a nearly normal testicular structure in an XXY chromosome-bearing individual until the age of puberty, when the testicular pathology that is characteristic of the Klinefelter syndrome develops rapidly (49). The Y chromosome of the mouse has also been shown to bear male-determining factors (50). But the details differ in the two species, for the XO sex chromosome arrangement results in a fertile female in the mouse and an infertile female in man.

The view that the sex chromatin is an XX chromosome marker is consistent with an XXY-complex for patients with Klinefelter's syndrome and a female chromatin pattern, and with an XO arrangement for patients with Turner's syndrome and a male chromatin pattern. But the important significance of the recent observations on chromosomal abnormalities is the clear demonstration of aneuploidy as a cause of some developmental errors in man. The next few years are certain to bring developments of the first importance in the field of human cytogenetics and in the application of cytogenetics to certain aspects of clinical medicine.

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Intercellular Activities in Vertebrate Development

Problems of embryonic organization are being attacked at subcellular, cellular, and supracellular levels.

Jane Oppenheimer

It is a historically fascinating but in some ways scientifically worrisome phenomenon that one of the principal problems currently under study by investigators of embryology is very much the same as one posed by Aristotle nearly 2000 years ago. Aristotle asked, in a passage that has lately been frequently quoted: "How, then, are the other parts [of the embryo] formed? Either they are all formed simultaneously—heart, lung, liver, eye, and the rest of them—or successively. . . . As for simultaneous formation of the parts, our senses tell us plainly that this does not happen: some of the parts are clearly to be seen in the embryo while others are not. . . . Since one part, then, comes earlier and another later, is it the case that A fashions B and that it is there on account of B which is next to it, or is it rather the case that B is formed after A?"

Is it the case that A fashions B and that it is there on account of B which is next to it, or is it rather the case that B is formed after A? This is the problem of becoming; how does what is one thing become what is apparently another? Does it become, or was it arrived the whole time, only finally, like Mephistopheles in the melodrama, tossing off its dark cape and domino to reveal its original self?

Aristotle approached the problem in terms of organs: "I mean, for instance," he wrote in continuation of the passage quoted above, "not that the heart, once it is formed, fashions the liver, and then the liver fashions something else; but that the one is formed after the other [just as a man is formed after a child], not by it." By placing his emphasis on organs, he recognized organization (though he did not call it by name) as

the primary clue to development and hence to the nature of the organism. Our very word *organism*, although in common use only since the 19th century, reflects the importance of the concept of organization in terms of organs which has dominated biology since the time of Aristotle.

Today the problems of development are attacked primarily at a cellular and subcellular level. Biologists of the mid-20th century believe that cells are the organs—to use the word in Aristotle's original sense of instrument—of development of the differentiating embryo. The most important aspect of development for the embryologist to study is the organization of the embryo. But since this has proved elusive, many investigators of development, though not all, have contented themselves with studying the primary elements of the embryo, the cells, and in turn their constituent parts.

The trends of thinking of embryologists are in some ways less highly organized than the morphogenetic activities of embryos, and it is hardly possible, therefore, to classify and neatly outline all the various methods currently being employed by embryologists to investigate all the varied methods employed by embryos to achieve their ends of making highly varied adults. The new tools of biological, biochemical, chemical, and physical sciences are being freely applied to embryological problems; the techniques of electron microscopy, of immunology and serology, of radiobiology, to name but a few, are being vigorously pursued in embryological laboratories. But even if it were desirable to list all the investigations currently exploiting such techniques, their results could not be—or at least have not been as yet—comprehended in a single

scheme of development which answers satisfactorily for all the questions of how the organization characteristic of the multicellular adult develops by means of cellular and subcellular activities out of the organization of the single-celled fertilized egg. (The development of the organization of the prefertilized egg, perhaps the most important developmental phase of all, is virtually uninvestigated.) Therefore, in order to narrow the scope of the present article to at least partially comprehensible dimensions, I shall confine this discussion to one or two problems of cellular activity in vertebrate development that have been under attack during the past quarter century and that still are today, in investigations that attempt to elucidate the most important unifying principle of development to have been discovered during the present century.

Around twenty-five years ago, Hans Spemann's Silliman Lectures first appeared in print, summing up the work of the previous quarter century on embryonic induction, a specific kind of cellular activity. What was the embryological setting when Spemann published his book? Wilhelm Roux had at the end of the 19th century postulated two possible alternative relationships between developing embryonic parts: (i) either they influenced their neighboring parts during development or (ii) they did not. It seemed at the outset very simple to choose between these alternatives, and he outlined an experimental program which would enable embryologists to do so. His own experiments were rarely adequate to answer the questions he framed, but the questions were nonetheless often appropriate ones, and Spemann and Harrison and their followers developed the techniques of transplantation and of explantation to investigate Roux's problems and their own which grew out of them.

One of the important first results of experimental embryology was that in which at the beginning of this century Spemann demonstrated a dramatic interaction between neighboring cell layers in the production of a complex structure, the vertebrate eye. A lateral outgrowth of the brain, the optic cup, which later forms part of the eyeball, was shown, by defect and transplantation experiments, to induce the overlying ectoderm, by touching it, to form a lens. In some experiments the ectoderm, which would normally have formed a lens, failed to do so in the absence of such contact; in others, flank ectoderm grafted over the optic cup at an appro-

The author is on the staff of the department of biology, Bryn Mawr College, Bryn Mawr, Pa.

appropriate time was able to form a lens, which it would not have done in its original position in the absence of contact with the optic cup. The ectoderm forms the lens in a very simple way: a circular patch of cells thickens, then separates off to lie below the rest of the ectoderm, which becomes skin. Enclosed by the iris, the lens rudiment will later elaborate the peculiar fibers which will become crystal clear for the transmission and focusing of light rays.

The lens-inducing effect is a general phenomenon, later found to occur in other vertebrate forms—certainly in birds, possibly in fish and mammals. The first demonstration of its occurrence in amphibians was, however, of prime importance in providing evidence for the development of the concept of embryonic induction.

It soon became apparent that other inductive systems have important roles to play during the course of amphibian development. Even more dramatic than the demonstration that an optic cup can induce flank skin grafted over it to form a lens was the demonstration that a circumscribed portion of the young amphibian embryo, the so-called organizer, which is located above the dorsal lip of the gastrula's blastopore, could when transplanted into another gastrula induce the formation of a more or less whole new embryo (Fig. 1). The organizer region comprises the primordia of the dorsal axial tissues (notochord, bilateral rows of skeletal muscles, head mesoderm). In the course of its inward movements during gastrulation, this region comes to underlay part of the ectoderm, which as a result of its contact with the underlying layer becomes a self-delineated area, the neural plate. The cells of the plate elongate, then form a canal whose walls meet and separate from the skin to form a tube. This is the segregated primordium of the central nervous system, which will undergo manifold processes of growth and change of form to become the brain and spinal cord; its tissue will differentiate all the highly varied cell types which carry on the complex functions of nervous action and reaction and integration. It is thus an important problem for the embryologist to try to ascertain what stimulus from the underlying axial tissue layer impels the future neural plate ectoderm to carry out the chain of events which leads to the production of the elaborate central nervous system.

Leaving aside for a moment the specific issue, to which we shall return, of the nature of the inductive stimulus,

we see that these experiments not only raised specific questions, as good experiments should, but that they also answered some general ones, as not all experimental results always do. They replied unequivocally in the affirmative, for some systems within vertebrate development at least, to Roux's question as to whether embryonic parts can influence other parts during development, and thus also to Aristotle's question as to whether A "is there on account of B which is next to it." Thus they were of the greatest theoretical significance, since they gave incontrovertible validity to the principle of progressive differentiation,

which holds that each step in development is an outcome of the steps immediately preceding it and a necessary condition for those which are to follow it.

While the principle of induction does not explain all developmental processes in all organisms, innumerable experiments have shown its wide applicability to many of them. The emergence of not only vertebrate lens and vertebrate nervous system but of many other organs of the vertebrate embryo can be understood only in terms of induction. While the differentiation of some organs in some invertebrates is accomplished independently of induction, inductive proc-

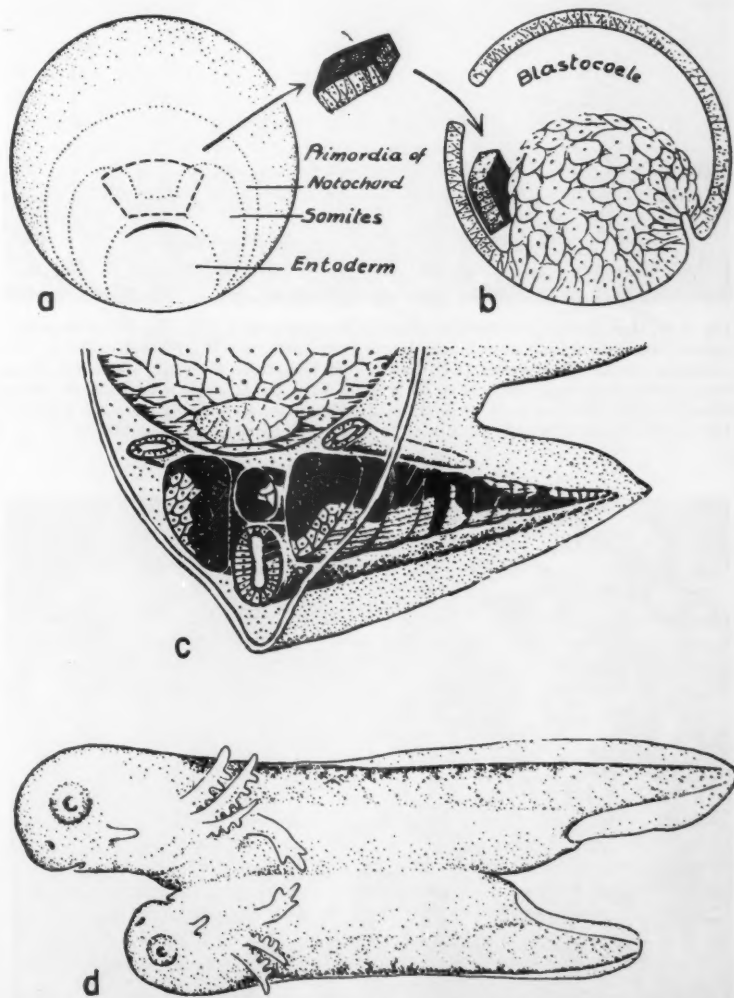


Fig. 1. Diagram of the transplantation of a piece of the amphibian upper blastoporal lip into another gastrula (a, b) and the structures self-differentiated and induced by the graft (c, d). In c, the tissues derived from the graft are shown in black, and the induced tissues, in white. The graft would probably be somewhat larger than shown if it were to induce an embryo as complete as that delineated in d. [From J. Holtfreter and V. Hamburger in *Analysis of Development*, B. H. Willier, P. A. Weiss, V. Hamburger, Eds. (Saunders, Philadelphia, 1955), p. 244, Fig. 82, reproduced by permission of Professor Holtfreter, the senior editor, and the publisher]

esses have been demonstrated to be responsible for the development of some organs in a number of invertebrates also. Embryologists agree that the exact character of the inductive mechanisms may

differ in detail at different stages in the forerunners of different organs. But the discovery of the general occurrence of the phenomenon was one of the most momentous discoveries of 20th-century

biology and was a factor of great importance leading to the recognition of the central position of problems of development in 20th-century biological thought and investigation.

To return to the specific question as to the nature of the stimulus by which one group of cells affects another during induction, it may be said at the outset that it has not yet been answered unequivocally for any single system, although the failure to arrive at a solution has surely not been for lack of trying, especially in the case of the induction of the amphibian nervous system, the problem on which the greatest amount of experimental attention has been expended.

At least one reason for the lack of final success in solving the problem was the adherence of embryologists to currently fashionable ways of thinking, which encouraged them to hope too early for too simple a chemical answer to too complicated an embryological, and hence an organizational, problem. Already in the early 1930's, chemical attitudes began to be assumed by investigators of embryonic organization. It was found at that time that killed organizer cells and also killed nonorganizer cells could induce the development of an amphibian nervous system, and next that tissues, sometimes treated and sometimes not, taken from varied organs of varied organisms, invertebrate as well as vertebrate, could cause inductions in the amphibian egg. Biochemistry was less advanced in the 1930's than in the 1950's—in fact the attempt to find the substance that could perform the miracle of organizing an embryo may have been one of the spurs to its rapid progress—and it seemed less naive then than now to ask: What is the substance that acts as the organizer? When Harrison gave his lecture at the Harvard Tercentenary in 1936 he could quote as quite appropriate the couplet from *Faust* in which Faust's pedantic student sang, "What used to be organized Now we can crystallize."

An early shattering of hopes resulted from the claims that a great diversity of chemical substances could act as inducers. Among the many substances demonstrated to produce inductions of sorts were a number of possible physiological significance; these included steroid hydrocarbons, fatty acids, proteins, including nucleoproteins, and nucleic acids. Indeed, embryology rendered another great service to biochemistry by calling attention to the possible significance of ribonucleic acids in protein formation

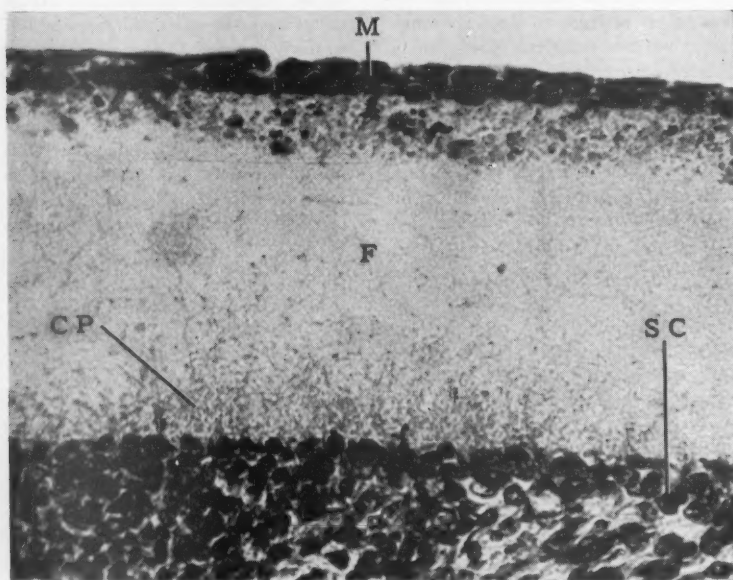


Fig. 2. Section through a culture in which mouse spinal cord (SC) has failed to induce tubule formation from mouse kidney-forming mesenchyme (M) through a filter (F), although cytoplasmic processes (CP) have visibly penetrated the filter. Weak inductions were produced through filters 20 to 65 μ in thickness but were largely eliminated when filters 80 μ in thickness were used. [From C. Grobstein, *Exptl. Cell Research* 13, 579, Fig. 5 (1957); reproduced by permission of the author, editors, and the publisher]

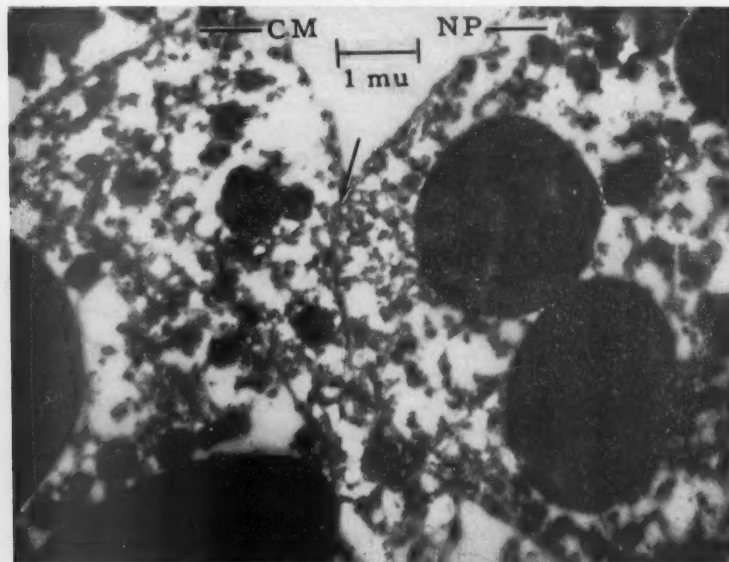


Fig. 3. Electronmicrograph showing process of neural plate cell (NP) in contact with process of chordamesoderm cell (CM) in an early neurula stage of *Xenopus*. The arrow points to the region of contact. [From R. M. Eakin and F. E. Lehmann, *Wilhelm Roux' Arch. Entwicklungsmech. Organ.* 150, 187, Fig. 13 (1957); reproduced by permission of Professor Eakin, the editors, and the publisher]

through Jean Brachet's histochemical studies on the localization of ribonucleic acid-rich particles in various regions of the amphibian embryo.

In view of the multiplicity of agents demonstrated to be able to induce the formation of the amphibian nervous system one might suppose that Harrison's successors delivering lectures today would find the quotation from *Faust* less apposite. Yet there are many for whose articles even now Goethe's lines might form a fitting rubric. It was perhaps historically inevitable that investigators in the early 1930's should have attempted to pinpoint a specific chemical agent as "the organizer"; while it may be equally inevitable, it is puzzling that the search for one, or for a few such agents, continues almost as vigorously today. This attitude is somewhat questionable from the biochemical point of view, since the biochemists themselves now seek to characterize the activities of cells in terms of metabolic systems rather than of special substances per se. Making the jump, however, from organizer to chemical substance is even less excusable on the strictly biological side, since "the organizer" is by definition a whole district of living cells and not at all any kind of substance extractable from this district. Embryologists who keep in mind the complexities inherent in the processes of organizing the development of an embryo are well aware of the fallacy of attributing the control of such organization to the presence of a single omnipotent chemical substance as such.

The search for chemical substances able to influence differentiation in the amphibian has altered in some respects, in that some of the effective agents now being isolated seem to induce ectodermal and others mesodermal structures, some anterior and others posterior ones. A merit of this change in attitude is that it is no longer generally considered to be a single magic substance that induces a nervous system or even organizes a whole embryo, but rather a number of substances that can affect cellular differentiation, at least *in vitro*. Nonetheless the significance of the varied agents currently under investigation remains a matter of some confusion.

The agents studied are being isolated not from the embryo itself but from fractions of highly complex organs or tissues, such as mammalian liver or kidney. Other sources of effective fractions—bone marrow, whole blood, blood serum, plasma, homogenized 9-day chick embryos—are also hardly to be described

as physiologically or biochemically simple or homogeneous. While no evidence has as yet been adduced to prove that agents corresponding to those in the effective fractions of liver, kidney, bone marrow, and so forth actually exist in the developing embryo, one group of experiments has suggested that an effective agent may be produced by amphibian chordamesoderm cells growing in tissue culture. It has been claimed that this agent is ribonucleic acid, and the evidence points to the fact that at least some of the effective agents extracted from the complex organs and tissues under analysis may be nucleoproteins or

nucleic acids. Many investigators consider this line of investigation to be one of the most promising currently being followed, and it is to be hoped that it will lead to further clarification of inductive mechanisms.

If, however, ribonucleic acids are as important for the synthesis of proteins as modern biochemistry suggests, it would be surprising if the suitable administration of ribonucleic acid or ribonucleoprotein to an embryo were not to result in some alteration of its development, provided it succeeded in entering its cells at all. But the fact that the alteration takes the form of making a new ner-

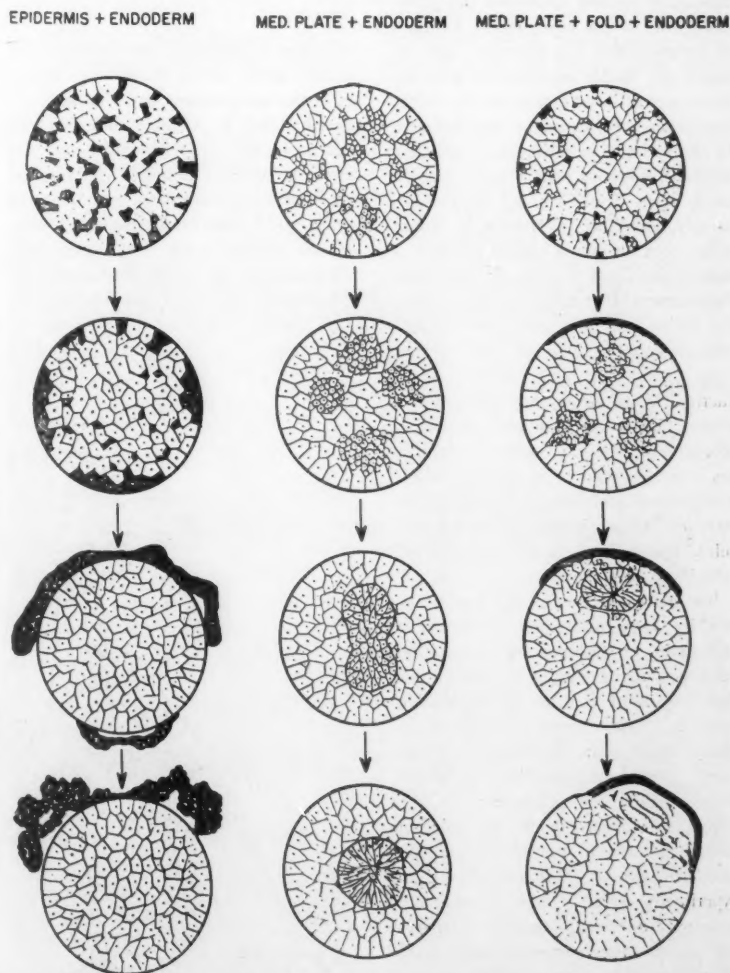


Fig. 4. Diagrammatic sections showing successive stages of reaggregation of experimentally dissociated cells of amphibian neurulae. (Left) The recombination of dissociated epidermal and endodermal cells leads to a sorting-out and self-isolation of homologous tissues. (Middle) When dissociated neural plate and endoderm cells are recombined, the former move centripetally to produce a solid core of neural tissue. (Right) Inclusion of neural fold cells with neural plate and endoderm results in the formation of epidermis and mesenchyme which prevent central allocation of the neural tissue and promote the formation of a cavity in the nervous tissue. [From P. L. Townes and J. Holtfreter, *J. Exptl. Zool.* 128, 79, 74, Figs. 18, 16, 17 (1955); reproduced by permission of Professor Holtfreter, the editor, and the publisher]

vous system or a new embryonic axis is attributable as much to the responding cells as to the administered ribonucleic acid or ribonucleoprotein. The nature, biochemical or physiological, of the processes whereby the reacting cells respond to the administration of ribonucleic acid, ribonucleoprotein, or any other inducing agent is something that embryologists realize it is important to know but an area they have as yet not been able to investigate.

Furthermore, whether indeed any large molecule actually passes from inducing to responding cells remains another open question, and one which unfortunately tracer techniques have not as yet been sufficiently refined to answer unequivocally. One of the more recent pastimes of embryologists has therefore been to search for visible mechanisms whereby substances of large molecular size might pass from the inducer to the induced. In one series of experiments in which a different inductive system from that we have been describing is employed—namely, an effect of embryonic mouse spinal cord on mouse kidney tubule formation in tissue culture—it has been demonstrated that a filter of known pore size which fails to permit protoplasmic contact between inducer and induced (Fig. 2) still permits at least weak inductive effects. In another study, protoplasmic continuity between amphibian chordamesoderm and overlying ectoderm has been suggested (Fig. 3); this the investigators postulate as a possible pathway for the exchange of macromolecules, lipid droplets, or even formed cytoplasmic elements.

But meantime, while the search for effective large molecules or molecular aggregates of fashionable composition continues, together with the search for their means of transfer by fashionable methods, some skeptics continue to worry about some experiments whose results seemed most unfashionable at the time of their first discovery. In the 1940's, an old experiment, the isolation in salt solution of amphibian gastrula ectoderm without chordamesoderm—an experiment which could theoretically have only one result, namely, no nervous system formation—suddenly had, when carried out on a different amphibian species, a totally different result. Nervous system was formed. Furthermore, these results were found to be modifiable by the simple expediency of changing the hydrogen ion concentration of the solution. (Back in the 1930's, by the way, when the first chemical studies were made, F. G. Fischer, a col-

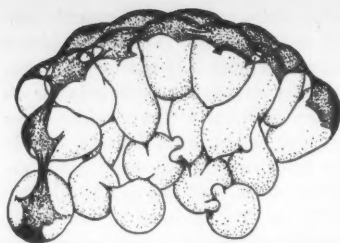


Fig. 5. Surface coat covering cells of the morula stage of *Amblystoma punctatum*. Filiform and knoblike processes can be seen interconnecting the blastomeres. [From J. Holtfrete, *J. Exptl. Zool.* 94, 265, Fig. 1 (1943); reproduced by permission of the author, editor, and publisher]

laborator of Spemann, had demonstrated nucleic acid, among many other agents of a dissimilar nature, to be an inducer, and had felt it probable that the acid components of the nucleotides were the effective agents, although the organic acids he found effective were large molecules and he had no success with hydrochloric acid.) In the new experiments performed in the 1940's the use of distilled water instead of salt solution, the addition of alcohol to the medium, or the absence of calcium ions also resulted

in the formation of nervous system by isolated ectoderm. The general significance of the new demonstration of nervous tissue differentiation by isolated ectoderm and the particular nature of the action of the environmental medium still remain to be satisfactorily interpreted. The experimental results were nevertheless of vast importance in that they proved the necessity of maintaining a skeptical attitude towards the conclusiveness of the results obtained with defined substances of complex nature as regards their inductive specificity. They pointed towards the fact that what determines the outcome of the experiment is not so much the nature of the applied chemical agents as the intracellular physiological mechanisms brought into play by the chemical stimulus, and thus they suggest the paramount importance of developing new methods, more adequate than the old, to investigate these mechanisms.

The fact that the embryologists who danced down the primrose way of biochemistry have failed to find within cells master molecular agents which govern the formation of embryos has not, however, perturbed some investigators who have meantime continued to study embryos at cellular and supracellular levels,

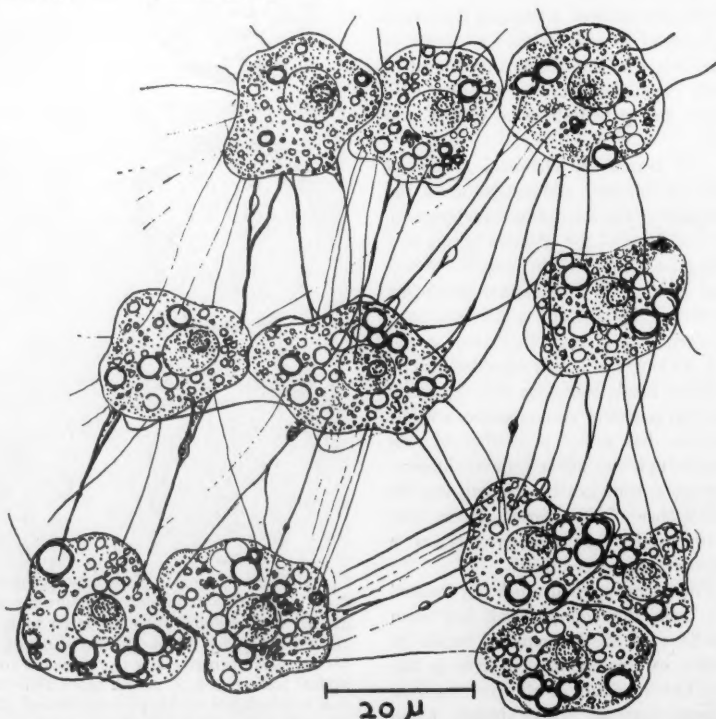


Fig. 6. Intercellular fibers joining living segmental plate cells at the definitive streak stage in the chick. [Courtesy of Nelson T. Spratt, Jr., University of Minnesota]

and from the laboratories of the latter are appearing results as dramatic as any which have ever been described for embryological experiments. Analysis involves resolution into elements, and the embryo's primary elements are cells. Embryos can now be physically as well as intellectually resolved into their cells, by treatment with trypsin or other dispersing agents, and the actions whereby such dispersed cells show affinities or disaffinities for each other, differing for different cell types and at different ages, are now being described (Fig. 4). The analysis of the factors responsible for such affinities and disaffinities has scarcely begun but promises fertile problems for investigation by modern immunological and other methods.

Finally, to conclude with the most important consideration of all, even in embryos such as those of the vertebrates, and in our amphibian example, in which induction and other cooperative cellular activities are essential components of progressive differentiation, these cellular actions are not isolated mechanisms but are components of the over-all processes used by the embryo to make its whole self. The significance of organizer action is that when the organizer is grafted, it induces not only a neural axis but a more or less whole embryo. In the heat of the press for the isolation of chemical agents this has sometimes been forgotten by embryologists, but never by embryos, and what becomes induced in any given situation in many cases seems to reflect at least a strong attempt of the reacting embryonic part to create a new whole.

A few investigators have studied agencies involved in the production and maintenance of wholeness by studying activities not only between but also over and above cells, which permit cells to conjoin their activities. Some visible entities have recently been described which might act in such capacities. In the amphibian embryo Holtfreter has demonstrated a supracellular coat (Fig. 5) which serves to coordinate the movements of the cells during gastrulation. Intercellular bridges, said to contain endoplasmic reticulum, have been demonstrated in the embryo of the chick (Fig. 6) at somewhat later stages than those we have been discussing for the amphibian. However, no open channels between early developing embryonic cells, such as those which connect synchronously developing cells of postembryonic stages—for instance, mammalian spermatids and spermatocytes (Fig. 7) and cnidoblast-forming interstitial

cells of *Hydra*—have as yet been demonstrated.

But there are some embryologists who still believe that even if such bridges were to be demonstrated, and even if the composition of the molecules and molecular aggregates or formed bodies which might traverse them were known, the question still would remain open as to what organizes the cells to construct the bridges and to manufacture the agents which cross them and to create the necessary physical conditions to permit the development of wholeness in the aggregate of cells. Lest the reader misunderstand, this statement does not represent a retreat to the position of Driesch, who had to evoke a *deus ex machina* to explain the processes whose machinery transcended his understanding. It is rather an admission that if embryologists

know that cells are important elements of the embryo, they are not yet able to define organization itself in physiological terms sufficiently precise to permit its analysis by physiological methods.

Embryos, like embryologists, are made up of atoms and molecules. What is not known about embryonic organization is how chemistry relates to structure, as was pointed out in the two summaries of the recent McCollum-Pratt Symposium on the Chemical Basis of Development. Yet much positive progress has been made in analytical embryology during the past half century. The most perceptive embryologists, such as Roux, Harrison, and Spemann in the past and Holtfreter, working at present, have been clever enough to isolate a few separate mechanisms which have been at least partially resolvable into simpler proc-

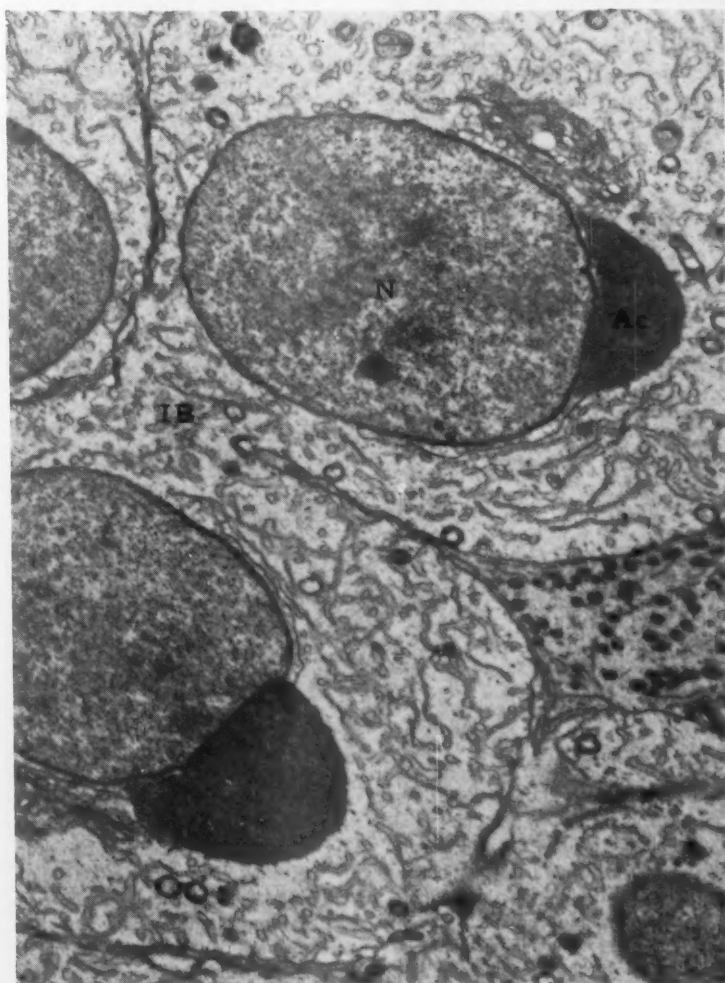


Fig. 7. Electronmicrograph showing intercellular bridge between two conjoined spermatids of the guinea pig. (IB) Intercellular bridge; (Ac) acrosome; (N) nucleus. [Courtesy of Don W. Fawcett, Cornell University Medical College]

esses. But the resolution into simpler processes has been partial, not complete, and the relation of the isolated mechanisms studied to the organization of the whole has thus far defied analysis and thus stands as a challenge to the embryologists of the future.

Wilhelm Roux was once asked by Emperor Franz Josef, who made a visit to his laboratory, how he made discoveries in experimental embryology. Roux replied that the investigator "must have a question in his mind, and then look for an appropriate method to force an unequivocal answer to it." Investigators have made great progress toward compelling an answer to the question raised by Aristotle, but the complete answer to it will never be known until a new Aristotle frames an equally cogent question or set of questions regarding the organization of the whole. Embryos are notoriously resistant to threats of force, and the new Aristotle, like the old, will surely be someone, who, like Roux, like Harrison and Spemann, like Holtfreter, understands the living whole embryo suffi-

ciently to deal with it on its own terms. Embryos are creative artists, and, like other artists, they create form. The difficulties that face whoever tries to explain their success have their counterparts in those confronting anyone who tries to account in specific terms for the greatness of any work of art. Knowledge of the molecular constitution of his pigments does not suffice to explain the genius of Leonardo. In embryology as in art, appreciation is probably more effective than atomizing as an introductory approach to the understanding of the genesis of form.

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Relationship between Stimulus and Response

The "shape" of the problem serves to clarify the disparity between graded and quantal response.

S. Loewe

In all sciences concerned with excitable biological systems, the task of quantifying the relationship between the excitatory stimulus and the biological response is complicated by the differences in excitability among the individuals studied. This article (1) tries to analyze the problems arising from this complication. As an almost uniquely suited proving ground for the analysis, the field of pharmacology has been chosen. This

field is entirely devoted to the study of a chain of events that begins with the pharmacological stimulus, called "dose" (D), and ends with the ultimate response to this stimulus, called "effect" (E).

The practical importance of the carriers of the pharmacological stimulus, the "drugs," has directed the efforts in this field toward an especially ambitious goal—namely, that of arriving ultimately at a single numerical expression of potency (P), the stimulatory strength inherent in a drug. The greater the effect E elicited by a certain dose D , the higher

the potency, and the greater the dose required to elicit a certain effect, the lower the potency:

$$P = f(E/D)$$

Hence, the student of potency sets out to measure the quantitative relationship between D and E . Very soon, however, he finds himself at a parting of the ways where one fork is marked "graded-response," the other, "quantal response." The road signs as well as the guidebooks may suggest that the two roads offer him an equal chance. Whether or not this conclusion is correct only a reliable road map will tell. Only a view of the *Gestalt* of the problem (2) will provide precise information on how closely akin graded and quantal responses are and on what role either of them plays in determining the dose-effect relationship and potency.

In such an endeavor, one must dispense with all and any procedures of transformation ingeniously introduced for biostatistical purposes—for example, with the use of metameters such as $\log D$, E probit, and logit. Any such metameter (3) is a mathematical function of the magnitude "as measured," a function "used in calculations" "because of its convenience" (the quotations are from Gaddum, 4) as a means of converting curvilinear into rectilinear rela-

The author is on the staff of the department of pharmacology of the College of Medicine, University of Utah, Salt Lake City.

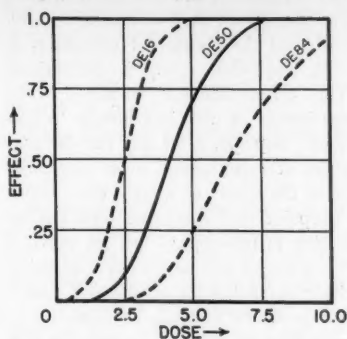


Fig. 1. Dose-effect curves. Curve DE_{50} is arbitrarily plotted on the basis of an assumed S-shaped course and of a tolerance value of 50. The two dashed curves for tolerance values of 16 and 84 were then calculated under the arbitrary assumption of constancy of the coefficient of variation at all levels of E .

tions (an instructive translation would be, "meta" equals "rubber," "meter" equals "band"). Whereas such orthopedic operations may excellently serve certain technical purposes, the faithful view, which I propose to display in this article, has to be drawn to scale and to depict the shape of the problem in all its natural curvaceousness.

Dose-Effect Curve

Customarily, the dose-effect relationship is graphically pictured in the form of the D,E curve which relates each dose D with its effect E in a diagram with the rectangularly intersecting coordinates of D and E (see the three arbitrarily plotted examples in Fig. 1). In all its simplicity, this form of presentation takes into account a number of noteworthy facts, such as (i) that the D,E relation is only a special case of stimulus-response relation, which again is a special case of cause-consequence relation; (ii) that D and E are continuously varying magnitudes; (iii) that D is the independent variable, whose conventional place is on the abscissa, and E the dependent variable, with its proper place on the ordinate. As to the yardstick of the two axes, D (the pharmacological stimulus) usually has the dimension of concentration. (grams per kilogram; moles per liter, and so on) (5); the most general way of quantifying E (the change in physiological function) is to express it as a fraction of the maximal alteration of function that can be evoked by the optimally effective stimulus.

Variation of Tolerance

Though generally accepted, the concept of the D,E curve fits only the ideal case in which all individuals of the population of experimental subjects (organisms, tissues, cells, and so on) exhibit the same tolerance of the pharmacological stimulus. In reality, the individuals in any population differ in tolerance T . When large, randomly selected populations are tested in single-dose groups, the percentage of responders at any selected E level increases with the dose and, hence, can be taken as a measure of T . The value n of T for any particular D can be regarded as the tolerance of the n th individual in a population of 100 individuals arrayed in series of increasing tolerance (6).

Thus T enters the graphic view as a third variable whose axis is suitably presented horizontally at right angles to both a vertical E axis and a horizontal D axis. The result is a D,T,E space octant rising over a basal D,T plane. For every value of T there rises a vertical

D,E plane containing a D,E curve of somewhat different course (compare the three curves, for T_{16} , T_{50} , and T_{84} , plotted in Fig. 1). It is only in such a three-dimensional octant that the D,E relationship can be faithfully depicted. The real D,E relation is not shown by a single D,E curve but is represented by the integration of the D,E curves for all the different values of T into a D,T,E space surface. A model of the three-directionally curved surface, constructed from the values given in Fig. 1, is depicted in Fig. 2.

Isographic Views

For a more concise clarification of certain aspects of the spatial arrangement, the stereometric image can be reduced to two-dimensionality by way of parallel projections of suitable profile lines of the space structure upon the three border planes of the space octant. In the context of this study, only those two projection planes involving the vari-

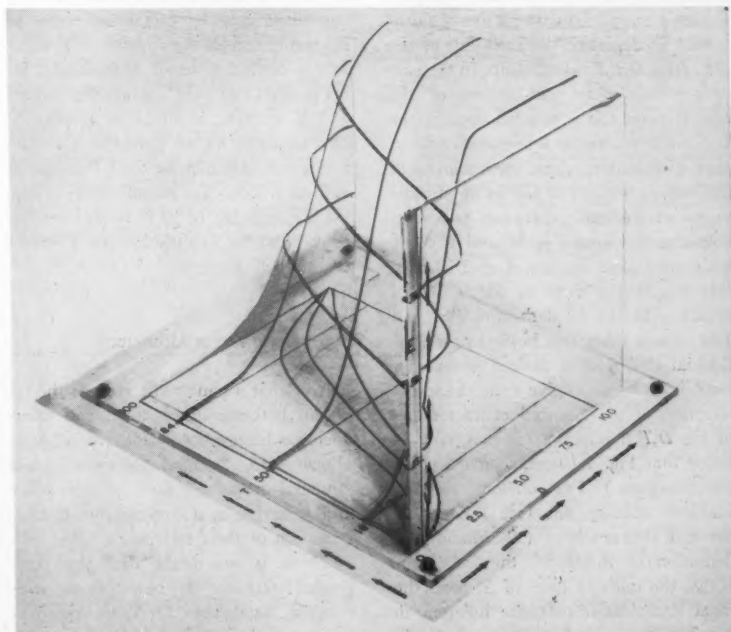


Fig. 2. Model of D,T,E space surface depicting the relationship between dose, tolerance, and effect. D , dose in values from 0 to 10 (mg/kg); T , tolerance in values from 0 to 100 (maximum tolerance); E , effect, marked in values of 0, 0.25, 0.5, 0.75, and 1.0 (maximum). The surface is constructed on the basis of the values employed in Fig. 1. The three curves rising with the slope of the space surface from its bottom to its top represent the dose-effect curves (isopleths) for tolerances 16, 50, and 84 respectively. Figure 1 shows their projections upon the vertical frontal border plane of the model. The three horizontal curves running from front to rear of the space surface represent the dose-tolerance curves (isobols) for effect levels 0.25, 0.50, and 0.75, respectively; their projections upon the basal D,T plane are visible in the lower half of this figure and also in Fig. 3. Note the complete disparity between the two types of curves.

able D are of interest—that is the vertical D,E and the horizontal D,T planes. In both planes the profile lines depict the relation between each two of the variables, the value of the third variable being constant along each curve and appearing only as its affix.

In an exhaustive projection picture, the profile lines would appear as an infinitely large family of curves—namely, of D,T curves and D,E curves, respectively. Discussion of such projection curves is facilitated by the general terminological usage designating them as *isograms* in reference to the third variable. Thus, the D,T , (E constant) curves in the D,T plane are designated by the term *isobol*, a word long employed (7) to name, in a map of any two variables, lines going through points of equal effect. No less appropriately, the term *isopleth* (taken over from geological maps where it is employed to designate lines going through points of equal content of an element) can be applied to any D,E , (T constant) curve in a D,E plane, along which the percentage of responders is equal.

It would be convenient if these still rather complex profile pictures could be further streamlined without loss of faithfulness in depicting the essentials of the respective D,T,E relationship. In the case of the isoplethic presentation of the D,E relation this is possible because the D,T curve represents a cumulative tolerance distribution where the majority of individuals is likely to fall in the middle range of tolerance, between two suitably chosen values $T < 50$ and $T > 50$, with maximum likelihood at $T50$. For this reason the isopleth for $T50$, together with the isopleths for $T16$ and $T84$ or any other two isopleths marking fiducial limits for a desired probability level, is quite apt to give a shorthand description of the essential characteristics of the D,T,E relation. (It may now be noted that Fig. 1 presents such a triple isoplethogram.) For obvious reasons, multiple isobolograms (see Fig. 3) do not lend themselves to a shorthand condensation of this type; the isobol for $E 0.5$, the midway level of E , lacks the focal statistical importance inherent in the $T50$ value, and no other short cut has yet been devised.

Floor Plans Supplement Vertical Profile Plans

That all three variables, D , T , and E , must inevitably be taken into consideration in every dose-response problem is

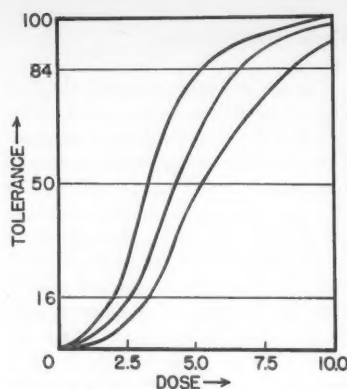


Fig. 3. Dose-tolerance curves at effect levels 0.25, 0.50, and 0.75, respectively, plotted on the basis of the data that underlie Figs. 1 and 2.

most clearly borne out by the procedural requirements arising when the picture of the general interdependency has to be replaced by the portrait of any individual case—that is, when the quantitative relations have to be expressed in concrete numbers. Even for a single D,E curve, of necessity isoplethic, the D value coordinated to a certain E value can accurately be established only by determination of the isobolic D,T curve at the desired E level. Accordingly, for a portrait of the three-dimensional D,T,E surface, a sufficient number of D,E isopleths for all pertinent T values and a sufficient number of D,T isobols at various E levels are equally prerequisite, the multiplicity of D,T isobols serving as the tool for establishing the T values of the D,E isopleths.

Spirit Level versus Altimeter

Now that a panoramic view of the relations between dose, effect, and tolerance has been unfolded, it is possible to allocate to "graded response" and "quantal response" their proper place and to arrive at a comparative characterization of their relations to D .

There is no doubt that the term *graded response* is synonymous with effect E , as defined for the purpose of the present analysis; the relation between dose and graded response is identical with the D,E relation envisaged in the preceding discussion.

The expression *quantal response* is not so self-explanatory. However, every description of the procedures employed in the study of quantal response makes it clear that first of all "a certain reaction" (8)—"some definite positive reaction"

(4)—is selected and that specified doses are then given, each to several individuals, and the number of responders in each single-dose group is determined. The "certain reaction" employed as the touchstone of the individual's "all-or-none" response, if of any use for purposes of quantitation, must necessarily be of the nature of what is often called "endpoint" (of effect)—a term not referring to the upper "end" of the D,E curve but to any selected and quantitatively defined point on the D,E curve; it must signify a certain adequately constant level of E in the course of a D,E relation. (For the validity of this postulate it is irrelevant whether adequate definition of other E levels of this particular D,E relation is considered either negligible or technically impossible.) Thus, the relationship between dose and quantal response is identical with the D,T relation at a certain fixed value of E ; the student of quantal response establishes a single D,T isobol.

Evidently the comparison between the objectives of graded-response and quantal-response studies reveals differences that lie deeper than merely in the field of procedure.

1) Judicious studies of graded response accurately evaluate altitude and slope all along the D,T,E surface. Determinations of quantal response yield numerical information on the tolerance distribution at a certain arbitrarily or involuntarily fixed elevation of that surface. If a more pictorial comparison is permissible, the student of graded response tackles the steepest ascent of the D,T,E surface, whereas the student of quantal response moves somewhere at the slope of the surface on a strictly level path.

2) Quite contrary to E , the value of T is determined solely by the biological subject. At constant T , E is unilaterally dependent on D ; at constant E , the D,T relation describes the mutual interdependency of two independent variables. Thus, the role played by the respective two variables is essentially different in the dose-graded-response and the dose-quantal-response relation.

3) That the two phenomena, graded response and quantal response, are designated by the word *response* is not based on an essential similarity but on a merely incidental homonymy. In graded response, as in its customary use in physiology, the noun (correctly employed as a singular) is a term from the language of measuring; in quantal response it is a term from the language of counting (and would probably more correctly be

employed as a plural). The two meanings of *response*, one might add, are as unrelated as those of the word *freedom* in "freedom (meaning exemption) from thought" and in "freedom (meaning liberty) of thought."

Thus, from all aspects one arrives at the conclusion that graded response and quantal response are by no means essentially equivalent and that they are not mutually interchangeable approaches to the determination of the D, E relation. The single isobol, which is all that can be established by a quantal response, depicts the D, T relation at one (and only one) level of E and gives no information whatever on the D, E relation. Whereas a plurality of D, T isobols from different E levels serves as a tool in determining the D, E relationship, due regard being given to the variation of T , a solitary D, T isobol signifies, so to speak, only one out of many necessary manipulations with this tool.

Potency, a "Many-Headed Multitude"

Since the ratio D/E is a major determinant of potency, a broader view of the D, E relationship is liable to throw more light on the problems of potency as well. Neither D, E nor D, T curves can be expected to be rectilinear, nor can the D, T, E structure be a (mathematically) regular surface. Hence, "the potency of a drug" is *never* a singular. Even for the same quality of effect, potency varies with E as well as with T . A satisfactory image of the potency of a drug is as composite and as pluridimensional as the image of the D, E relationship. No

formula is yet available by which this infinite multitude of potency values can be compressed into a single figure.

Whenever the potency of a drug is presented in the form of a single value, this signifies that the value is valid only for a narrow section of the large field of varying potencies and has been obtained by keeping some determinant variables constant and thus disregarding them. In this way, for instance, quantal-response procedure unassumingly pin-points its attention on establishing a value $1/P$ called " ED_{50} ." In this expression, "50" indicates that the $1/P$ value offered is valid only for T_{50} —that is, for subjects exhibiting the median tolerance of the "normal" or "probit 5" individual. E in " ED_{50} " is usually said to stand for "effective"; the meaning is clearer if it is interpreted as standing for "endpoint"—namely, for the particular level of E on which the isobolic D, T relation of the quantal-response study takes its course.

Fortunately, as discussed above, a quantal-response study, in order to arrive at the ED_{50} value by biostatistical interpolation, must first establish a number of D values for other tolerances in the course of the D, T isobol and can thus increase, though still only on the same constant E level, the amount of information considerably by adding data on the "error" (error due to the variation of T)—for example, the ED_{16} and ED_{84} values. These fiducial limits are often determined by admirably intricate biostatistical calculations; however, such intricacy must not mislead one into believing that the ED_{50} marks more than a single point on the D, T, E surface, that the P value derived from it marks more

than one out of many different P values of the drug, or that the three ED values presented yield more than a still rather crude estimate of the tolerance distribution on the one particular E level. Nor must it divert attention from the fact that not even a much more exhaustively established D, T curve could give any information on potencies at other E levels. It is not necessary to emphasize that all these fallacies are avoided when the aforementioned graded-response studies of the real D, E relations, aided by studies of D, T relations at several E levels, are employed as the basis of multiple $1/P$ and P determinations.

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5. If some biostatisticians and even biologists tend to attribute to dose the dimension of weight, they forget what the derivation of the word (Greek: *dosis*, a giving) implies—namely, that the weight of the drug powder does not *per se* constitute a stimulus but only "in dependency on circumstances of person and organ" [E. von Weizsäcker, in *Beithe's Handbuch der Physiologie* (Berlin, 1926), vol. 11, p. 14],—that is, in appropriate contact with the excitable substrate.
6. The term *tolerance* is employed here in preference to the closely related term *threshold*. Both are reciprocal functions of sensitivity; however, tolerance can be characterized as referring to the step from negative to positive response at any of a wide range of E levels, whereas the word *threshold* may be understood to refer only to the doorsill between lack of any response and the minimal perceptible E level.
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(other than textbooks for class use) under the provisions of Title III of the National Defense Education Act of 1958.

Initially, United States book publishers provided complimentary copies of books on a preliminary list, which was then circulated for review and evaluation to members of the AAAS Council. Not only have all of the books listed been suggested by specialists, but, to assure their suitability, they have been read and evaluated by senior high-school students and college undergraduates already well grounded in the various fields of science and mathematics.

Each citation in the AAAS catalog contains a brief descriptive note and a designation concerning degree of difficulty. To assist librarians with limited

News of Science

AAAS Library Program Releases Book List: Elementary-School Traveling Library Launched

The AAAS Library Program, with support from the National Science Foundation, has this year issued a new catalog, *The AAAS Science Book List*, containing 900 titles. The new 140-page publi-

cation is a guide to recreational and collateral reading and to basic reference works in the sciences and mathematics for junior and senior high-school students, college undergraduates, and non-specialist adults. It also serves as an acquisition guide for school and public libraries. The list has been prepared specifically as an aid in purchasing books

budgets, the AAAS has marked approximately 100 entries with a double asterisk to indicate books that are considered indispensable; some 200 other books carry a single asterisk to indicate that they are recommended if resources permit.

While several well-known book lists for high-school libraries are available, none of those consulted by Hilary Deason, director of the AAAS Science Library Program, gave sufficient representation to the sciences and mathematics. Deason believes that in the average high-school library the titles in the pure and applied sciences should aggregate at least 20 percent of the total. However, a survey of the libraries of approximately 2600 representative high schools participating in the Science Library Program during the past 2 years shows that science titles constitute only 5.2 percent of their collections.

Primary-School Library Launched

On 7 September the National Science Foundation announced the award of a \$500,000 grant to the AAAS to extend the successful Traveling High-School Science Library Program to include a Traveling Elementary-School Science Library. Five hundred sets of 160 books have been selected for the new program and, as schools reopen this month, students in 800 elementary schools throughout the nation will begin to enjoy science books of the kind heretofore circulated only in high schools.

The 160 books represent all major scientific disciplines, including mathematics. An accompanying catalog classifies the volumes at three levels of difficulty: *P*, primary or very simple; *I*, intermediate; and *A*, advanced. The AAAS plans to circulate 80 books at a time to each of the 800 schools, with an exchange at mid-year.

High-School and Paperback Programs

The Traveling High-School Science Library is now beginning its fifth year, having been instituted in 1955-56 with 11 sets of books that circulated to 55 schools. This year the library contains 465 200-book sets that will go to 1700 schools. Each of the current units consists of 165 books that were included in the library in previous years and 35 new selections, necessary because certain books included previously became unavailable.

Two years after the establishment of the first Traveling Library it became evident that the program was stimulating

wide interest among adults; therefore, *An Inexpensive Science Library*, a selected list of paperbound science books, was prepared. A first edition of 24,000 copies issued in 1957 and a revised second edition of 50,000 copies issued in 1958 are both out of print. The present edition contains a brief descriptive note for each book and classification according to degree of difficulty. The edition lists 400 titles.

The AAAS publishes annotated catalogs of the two traveling school libraries mentioned above, which may be obtained at 25 cents each; *The AAAS Science Book List* is \$1 a copy; and *An Inexpensive Science Library* costs 25 cents.

Senate Committee Reports Effects of Hypothetical Nuclear War

A "Summary-Analysis" of hearings on biological and environmental effects of nuclear war was released on 31 August by the Joint Congressional Committee on Atomic Energy. The publication reviews the major points developed during hearings that were held 22-26 June by the Special Subcommittee on Radiation, under the chairmanship of Representative Chet Holifield (D-Calif.).

The hearings covered by the 58-page analysis were for the purpose of establishing "a public record clearly setting forth the scientific facts concerning the probable physical and biological effects of such a war on man and his environment." The analysis noted that "this is the first time any comprehensive presentation of such facts has been made to the American people or to the people of any other nation."

The subcommittee assumed a hypothetical attack in which 263 nuclear weapons in 1-, 2-, 3-, 8-, and 10-megaton sizes, with a total yield of 1446 megatons, were detonated on 224 targets within the United States. An additional 2500 megatons were assumed to have been detonated elsewhere in the Northern Hemisphere in attacks on overseas United States bases and in retaliation against the aggressor homeland. All weapons were arbitrarily designated as having a yield of 50 percent fission and 50 percent fusion.

The human casualty estimates and the probable damage to dwellings in the United States were described as follows:

"The expert testimony and supporting scientific data presented at the Subcommittee hearings indicate that under present conditions such an attack would

have cost the lives of approximately 50 million Americans with some 20 million others sustaining serious injuries. More than one-fourth (11.8 million) of the dwellings in the United States would have been destroyed and nearly 10 million others would have been damaged. Some 13 million additional homes would have been severely contaminated by radioactive fallout. Altogether, approximately 50 percent of existing dwellings in the United States would have been destroyed or rendered unusable for a period of several months.

"Although the weapon detonations used in this exercise were designated as surface bursts which would maximize the local radioactive fallout hazard, nearly 75 percent of the deaths would have resulted from the blast and thermal effects combined with immediate radiation effects. Only 25 percent of all fatalities would have resulted from fallout. At the same time more than half of the surviving injured would have radiation injuries. Most of the damage sustained by dwellings would have resulted from the blast and thermal effects."

The analysis also points out that "probably the most significant finding presented to the Subcommittee was that civil defense preparedness could reduce the radiation casualties of the assumed attack on the United States from approximately 25 percent of the population to about 3 percent." It was the conclusion of expert witnesses that the United States must have a national radiological defense system. The report especially emphasizes the finding that a nuclear war of the magnitude considered would not, as many had previously believed, extinguish all human and animal life.

AAAS Oceanographic Congress Has Large Attendance

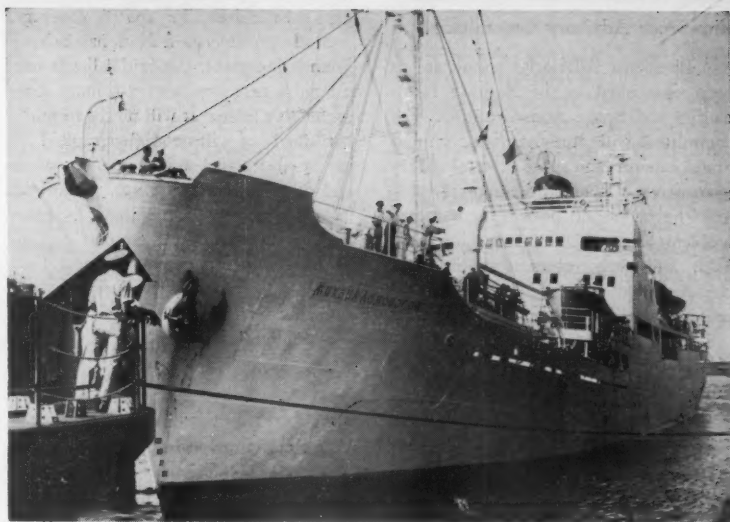
There were 41 scientists from the U.S.S.R. alone among the participants in the International Oceanographic Congress that closed at United Nations headquarters on 12 September. Nearly 1200 people, representing more than 40 countries, registered for the 13-day meeting, which was jointly sponsored by the AAAS, UNESCO's International Advisory Committee on Marine Sciences, and the Special Committee on Oceanic Research of the International Council of Scientific Unions.

There were 11 women in the Soviet group, which arrived on 28 August aboard the oceanographic ship *Mikhail*

Lomonosov, a large vessel that carries a 64-man crew. The Russians were welcomed by a AAAS delegation that included Gordon Lill, a member of the committee on arrangements and chief of the geophysics branch of the Earth Sciences Division, Office of Naval Research. He is shown here greeting Arkady Kolesnikov, head of the Soviet group.

The French ship *Calypso* was another of the research vessels that visited New York for the congress. The 360-ton converted mine sweeper carried a crew of 21 and a three-man scientific team headed by Jacques-Yves Cousteau, the ship's commander and director of Monaco's Oceanographic Museum.

In the *Calypso's* afterhold was a newly developed submarine vehicle, the "diving saucer," which was commissioned at Marseilles a month ago. This spheroid device that will hold two investigators was designed to study the Continental Shelf at levels down to 1500 feet. The vehicle is water-jet propelled and steered, and is balanced by mercury. Its jets, mobile nozzles lodged in finlike projections, are fed by a battery-operated pumping system. The diving saucer will be used in exploration for the first time in Puerto Rican waters towards the end of this month. Two men who helped develop the saucer were aboard the



Oceanographic ship *Mikhail Lomonosov* that brought 41 Soviet scientists to the recent AAAS-sponsored International Oceanographic Congress at the United Nations.

Calypso: André Laban, director of the French Submarine Research Center at Marseilles, and Jean Mollard, submarine engineer.

Every registrant at the International Oceanographic Congress received a 67-page program and a 1022-page volume containing preprints, each in two lan-

guages, of the 469 papers in the afternoon sessions. Additional copies of the preprints may now be obtained for \$7.50 each from the AAAS Business Office in Washington. Later, the AAAS will publish the 30 major addresses delivered during the morning sessions as part of its *Symposium* series.



(Left). Scientists and crew members aboard the *Mikhail Lomonosov*. (Right). Arkady G. Kolesnikov, chief of the Soviet group at the oceanographic conference, and Gordon Lill, head of the Geophysics Branch, U.S. Office of Naval Research.

Space Administration Establishes Bioscience Advisory Committee

A Bioscience Advisory Committee has been established by the National Aeronautics and Space Administration. The committee will study current United States capability in space-orientated life-science research and development; outline the scope of present and future problem areas in the space bioscience field; and then recommend the part NASA should play in future bioscience activity related to the space program.

Seymour S. Kety, chief of the Laboratory of Clinical Science, National Institute of Mental Health, is chairman of the new group, which has the following bioscientist members: Wallace O. Fenn, professor of physiology at the School of Medicine and Dentistry, University of Rochester; David R. Goddard, director of the division of biology, University of Pennsylvania; Donald G. Marquis, professor of psychology at Massachusetts Institute of Technology; Robert S. Morison, director of medical and natural sciences, Rockefeller Foundation; and Cornelius A. Tobias, professor of medical physics, University of California, Berkeley. Clark T. Randt, NASA scientist for space medical research, has been appointed executive secretary of the committee.

Union List of Abstracted Periodicals

Among the first projects initiated by the newly established National Federation of Science Abstracting and Indexing Services is the compilation of a union list of periodicals covered by the major U.S. abstracting and indexing services. The planned list will indicate for each periodical: title, author (if a series), country, language(s), name of service providing coverage, and type of coverage—that is, complete, partial, or monitored; abstracts, critical reviews, or indexes only.

At present, more than 10,000 scientific serials are being received by U.S. libraries. Many of these are abstracted, wholly or in part, by several major or minor abstracting or indexing services; others are probably not being abstracted by any service. The preparation of the list will enable the abstracting services to determine: (i) where duplication of coverage exists and whether such duplication could or should be avoided; (ii) where certain periodicals can be obtained by loan, or where photocopies of specific

articles can be obtained; and (iii) what gaps exist in over-all or specific coverage.

Made possible by a National Science Foundation grant, this initial list is considered a first step toward a more comprehensive listing. It will not be formally published but will be mimeographed for use by abstracting and indexing services and other interested groups. Additional information may be obtained by communicating with Mr. Raymond A. Jensen, Executive Secretary, National Federation of Science Abstracting and Indexing Services, 301 E. Capitol St., Washington 3, D.C.

Senate Committee Approves U.S. Participation in Century 21

Federal participation in the Century 21 Exposition in Seattle, Wash., in 1961 and 1962 won the approval of the Senate Foreign Relations Committee in a recent vote taken in executive session. Senator Warren G. Magnuson (D-Wash.) and Senator Henry M. Jackson cosponsored the legislation under consideration.

The proposed program calls for some 14 agencies of the federal government to exhibit their scientific accomplishments at the 18-month science, culture, and industrial fair, an international event that will have the theme "Man in Outer Space." The exposition is being sponsored by the city of Seattle and the state of Washington, which have so far put up some \$30 million in building, property, and operating funds.

The House Committee on Science and Astronautics already has approved a \$12.5 million program for federal participation in the exposition. The Senate version of the bill provides for "such funds as may be necessary."

Radar Telescope

A radar telescope with a parabolic reflector 142 feet in diameter is under construction at Stanford University. It will be completed in about a year. This will be the largest radar telescope in the United States and the second largest in the world. The transmitter will operate in the frequency range from 20 to 60 megacycles per second; it will be the most powerful ever built in this frequency range.

The project was announced recently by scientists of Stanford University and the Stanford Research Institute. It will be a joint undertaking by SRI's Com-

munication and Propagation Laboratory and the university's Radio Propagation Laboratory, with support from the Air Force Cambridge Research Center.

Usually radio telescopes are equipped to receive only naturally occurring electromagnetic radiation from the cosmos. With the high-powered transmitter it will be possible to transmit signals to nearby planets, such as Venus. This technique is becoming increasingly important in studies of the solar system. The Stanford group will attempt to obtain radar echoes from Mars and from the sun itself. This technique is called "radar astronomy," to distinguish it from "radio astronomy," which involves only reflection of natural radiation.

Some of the data the group expects to obtain are more accurate measurements of cosmic distances; data on the surface of the moon and planets; the rotation speed of Venus; ionization density and ion distribution in the sun's outer corona and around various planets; and data on the amounts and movements of ionized gases and space debris between the earth and the moon, and in interplanetary space.

Emigration of the Intelligentsia

Among the persons arriving as Soviet zone refugees at the emergency transit camp of Berlin-Marienfelde (West Germany) during the first 6 months of this year were 455 university professors and teachers from various types of schools, 443 engineers and technicians, and 161 physicians. The Bonn government's overseas information paper, *The Bulletin*, said of these refugees:

"Many of them not only held high, well-paid positions but also enjoyed other privileges not granted the average subject of the Soviet zone régime, since this régime hopes by especially good treatment to prevent the emigration of the intelligentsia.

"Nevertheless, the tendency to flee westward has increased among members of the very professions favored by the authorities and the Communist Party."

The Bulletin stated further that at Soviet zone universities many professorial chairs are no longer filled, and at hospitals there is a lack of specialists. The University at Halle-Wittenberg is cited as having lost 77 instructors to the West in the period from May 1958 to May 1959, and in a year the Dresden Medical Academy is said to have lost 10 percent of its staff, 17 of them specialists or senior staff members.

Grants, Fellowships, and Awards

Conservation. The National Wildlife Federation and its state affiliates offer a number of scholarships and fellowships to qualified individuals working in the field of conservation or conservation education. Activities included in these categories are teacher training; curricular problems; conservation workshop techniques; textbook development; and state programs. An applicant need not necessarily be enrolled in an institution of higher learning if his project or proposal has merit. Application blanks and further information may be obtained from Executive Director, National Wildlife Federation, 232 Carroll St., NW, Washington 12, D.C. Completed application forms must be submitted before 1 November.

General. The National Science Foundation has announced that approximately 1000 Cooperative Graduate Fellowships will be offered in support of graduate study in the sciences, mathematics, and engineering during 1960-61. In this second year of operation of the program, applicants may request fellowship support for study at one of 152 designated colleges and universities—those which are authorized to confer the doctoral degree in at least one of the sciences. (During the first year of the program there were only 115 designated institutions—those that had awarded a specified minimum number of science doctorates.) Applicants should apply through the participating institution of their choice.

Tenures of 9 or 12 months are optional with the recipient. Fellows will receive a basic annual stipend of \$2200 from funds provided by NSF and will be encouraged to undertake limited teaching responsibilities. The institutions themselves, at their discretion, may supplement the stipend by as much as \$800 for a fellow on a full year's tenure or \$600 for those on the shorter tenure. In lieu of tuition and fees, the foundation will provide each institution with a predetermined and standardized cost-of-education allowance on behalf of each Cooperative Graduate Fellow. This program, in which the first awards were made in March 1959, is supplementary to the foundation's continuing Graduate Fellowship Program.

Application materials may be obtained from the graduate dean of a participating institution or from the Fellowships Section, Division of Scientific Personnel and Education, National Science Foundation, Washington 25, D.C. Appli-

cations must be submitted to the graduate dean of the participating institution of the applicant's choice by 6 November.

Tropical medicine. Fellowships in tropical medicine and parasitology are being offered by the Louisiana State University School of Medicine within the framework of a training grant from the National Institute of Allergy and Infectious Diseases. This program is now in its fifth year, having been supported by the China Medical Board of New York, Inc., during its first 3 years.

These fellowships are available to those holding a Ph.D. or M.D. degree and to advanced Ph.D. candidates. Prospective participants must be affiliated with an accredited university or college. They must have teaching or research duties, or both, in some field of medicine involving problems pertaining to a tropical environment.

Fellows in the program spend 8 weeks in either Central America or the Caribbean area. Opportunities are provided for collecting specimens for teaching purposes. Groups leave New Orleans in October, January, April, and July each year.

Fellowships are also available for periods of from 3 to 12 months. Such a long-term fellowship may be awarded to an individual who needs more time for research training because of special teaching responsibility in some field of tropical medicine. For further information and application blanks, write to George A. Thurber, Office of the Dean, Louisiana State University School of Medicine, 1542 Tulane Ave., New Orleans 12, La.

News Briefs

The House and Senate have approved a bill to award a National Medal of Science for outstanding contributions in physical, biological, mathematical, and engineering sciences. In the final version of this bill (H.R. 6288), medal winners will get no cash awards. The version of H.R. 6288 approved by the House Committee on Science and Astronautics would have awarded each medal winner a tax-free stipend of up to \$10,000.

* * *

The National Cancer Institute has just published the first directory of its research fellows to appear since the fellowship program was established in 1937. The 134-page publication contains a brief statement about each of 924 fellows. It also discusses the history of the

program, which was the first of its kind to be supported by the federal government. A limited number of free copies are available from the National Cancer Institute's information officer. Copies may also be obtained from the Superintendent of Documents, Government Printing Office, Washington 25, D.C.

* * *

A 2-week course in nuclear safety will be offered by the Atomic Energy Commission beginning 21 September in Oak Ridge, Tenn. The commission is providing the course on techniques of handling fissionable materials because such training is not available through established educational organizations and because industrial firms actively engaged in the expanding nuclear-energy industry have requested training in this field for their personnel. The course will be limited to 100 participants.

* * *

A new international scientific organization, the American Society of Pharmacognosy, was announced last month by Edson F. Woodward, temporary chairman of the group. The society was formed by 150 pharmacognosists attending meetings at the University of Illinois' Chicago Professional Colleges. For information write to Frank L. Mercer, St. Louis College of Pharmacy, St. Louis, Mo.

* * *

The Darwin Centennial Committee of the University of California, Santa Barbara, has completed plans for a series of lectures this fall commemorating the centennial year of the publication of Darwin's *Origin of Species*. A phase of Darwin's influence will be discussed by each of the following distinguished scholars: John Herman Randall, professor of philosophy at Columbia University; George W. Beadle, Nobel laureate and professor of biology and chairman of the department at California Institute of Technology; Albert Hofstadter, professor of history at Columbia University; Robert E. Fitch, professor of Christian ethics and dean of the Pacific School of Religion in Berkeley.

* * *

A volume of lectures by distinguished scientists on problems associated with manned satellites and space operations, which were presented before the staff of the Office of Naval Research and representatives of other government agencies during 1958, may be obtained for \$2.50 from the Office of Technical Services, U.S. Department of Commerce, Washington, D.C.

Scientists in the News

ALBERT C. SPAULDING, on leave of absence from the University of Michigan where he is associate professor of anthropology and curator of archeology at the Museum of Anthropology, has been appointed program director for anthropology and history and philosophy of science, Office of Social Sciences, National Science Foundation, Washington, D.C.

MERRIL EISENBUD, manager of the U.S. Atomic Energy Commission's New York Operations Office, has been appointed professor of industrial medicine at New York University Post-Graduate School of Medicine. He will assume direction of a new laboratory concerned with the study of long-range effects of radioactivity on man, which will be established at the university's medical center.

ROY E. ALBERT, assistant director of the Radioisotope Laboratory of George Washington University Hospital, Washington, D.C., and an associate of Eisenbud at the Atomic Energy Commission, has been appointed associate professor of industrial medicine at New York University Post-Graduate School of Medicine.

CURT P. RICHTER, professor of psychobiology at the Johns Hopkins Medical School and director of the Psychobiological Laboratory at the Phipps Psychiatric Clinic in Baltimore, Md., will deliver the two Thomas William Salmon lectures at the New York Academy of Medicine on 2 December. His subject will be "Biological Clocks in Medicine and Psychiatry."

Various scientists from the United Kingdom are now visiting in the United States, or will arrive shortly.

S. N. CURLE, senior scientific officer, Aerodynamics Division, National Physical Laboratory, Teddington, will arrive 29 September and deliver a lecture at the Anglo-American Aeronautical Conference in New York, 5-9 October. He will also visit Boston and Providence; he will leave the country 10 October.

W. H. GLANVILLE, director, Road Research Laboratory, Harmondsworth, will arrive 9 October and visit Washington, D.C., and Chicago. He will leave the country 22 October.

L. C. TYTE, director, Mining Research Establishment, National Coal

Board, London, will arrive 21 September to attend the International Conference of Directors of Mines Safety Research, Pittsburgh, Pa., 28 September-2 October. He will also visit Washington, D.C. (23 and 24 September), Colorado, and Ottawa, Canada. He will leave 16 October.

R. V. PITT-RIVERS, a member of the Medical Research Council's scientific staff at the National Institute for Medical Research, Mill Hill, London, arrived 2 September to spend 6 months in the Clinical Endocrinology Branch of the National Institute of Arthritis and Metabolic Diseases, Bethesda, Md., and 1 month visiting other centers. She will also present a paper at a conference of the New York Academy of Sciences on "Modern Concepts of Thyroid Physiology," 5-7 November.

The following scientists will receive honorary degrees on 29 September at ceremonies celebrating the centennial of the founding of the Northwestern University Medical School.

CHARLES BEST, professor of physiology at the University of Toronto.

HORACE W. MAGOUN, professor of anatomy at the Medical Center of the University of California, Los Angeles.

IRVINE McQUARRIE, director of research at the Bruce Lyon Memorial Research Laboratory of the Children's Hospital of East Bay, Oakland, Calif.

JOE VINCENT MEIGS, clinical professor of gynecology at Harvard University.

I. S. RAVDIN, chairman of the department of surgery at the University of Pennsylvania.

WILLIAM S. TILLET, professor of medicine at New York University College of Medicine.

SHIELDS WARREN, professor of pathology at Harvard University.

CONRAD ELVEHJEM, president of the University of Wisconsin.

Scientific visitors from Australia to the United States include the following:

W. R. BLEVIN, research officer of the Division of Physics, Commonwealth Scientific and Industrial Research Organization, arrived 13 September and will leave 13 October. His itinerary includes Washington, D.C., Maryland, Virginia, New York, Connecticut, Rhode Island, Massachusetts, and California, and Ottawa, Canada.

A. J. FARNWORTH, principal research officer, Division of Textile Industry, Commonwealth Scientific and

Industrial Research Organization, will arrive 24 September and will visit California, New York, New Jersey, Washington, D.C., Delaware, Massachusetts, North Carolina, and Louisiana. He will leave the country 25 October.

GEORGE G. OBERFELL, retired vice president in charge of research and development of the Phillips Petroleum Company, Bartlesville, Okla., will receive the Walton Clark Medal of the Franklin Institute, Philadelphia, Pa., on 21 October.

Recent Deaths

AARON BELL, New York, N.Y.; 57; practicing neuropsychiatrist; psychiatrist of the New York State Department of Mental Hygiene; former director of neuropsychiatry at Lenox Hill Hospital; 26 Aug.

A. HASTINGS FISKE, Woodside, Calif.; 65; pharmacist and retired vice president of Eli Lilly and Company; 25 Aug.

CHARLES FAMA, New York, N.Y.; 70; specialist in internal medicine; former director of Westchester Square Hospital; 29 Aug.

GEORGE E. GIBSON, Richmond, Calif.; 74; retired professor of chemistry of the University of California, Berkeley; specialist in thermodynamics and physical chemistry; 26 Aug.

ISTVAN GYORFFY Székesfehérvár, Hungary; 78; bryologist and retired professor of botany of the University of Kolozsvár and the University of Szeged; editor of *Folia Cryptogamica*; 16 Apr.

LEROY A. HOWLAND, Middletown, Conn.; 80; retired in 1947 as dean and Fisk professor of mathematics of Wesleyan University; had been vice president and acting president of the university; 26 Aug.

ARTHUR F. TAGGART, Scarsdale, N.Y.; 74; Vinton professor emeritus of mining at Columbia University; author of *Handbook of Ore Dressing and Manual of Flotation Processes*; 22 Aug.

HAROLD S. VANCE, Washington, D.C.; 69; Atomic Energy Commission member since 1955; former chairman of the executive committee of the Studebaker Packard Corporation; 31 Aug.

STEPHEN N. WYCKOFF, Berkeley, Calif.; 68; retired forest scientist of the U.S. Forest Service; executive vice president and one of the founders of the Forest Genetics Research Foundation; 1 Sept.

Book Reviews

The Astronomer's Universe. Bart J. Bok. Melbourne University Press, Melbourne; Cambridge University Press, New York, 1958. xi + 107 pp. Illus. + plates. \$3.75.

This book is based on four lectures on modern astronomy given by Bart J. Bok at the Australian National University in October 1957 and repeated at the School of Physics of the University of Sydney in January 1958. The lectures were on an elementary level and were descriptive in nature. The book is intended for readers with little previous knowledge of astronomy.

Bok covers four topics: (i) The solar system, (ii) The stars as individuals, (iii) The Milky Way galaxy as a stellar system, and (iv) The ages and evolution of the stars.

Without question, astronomy is today passing through a renaissance. As Bok states in his opening sentence, "Astronomy is on the move." This is due mainly to new instrumentation and to the beginnings of a theory of stellar evolution which permits the ordering of many of the observational facts of stellar systems.

Developments since 1946 have lent an excitement to astronomy which is basically different from and far removed from spectacular rocket technology and possible space travel. Present-day astronomy at last seems to be reaching toward an understanding of the formation and evolutionary processes of the universe as a whole. Astronomers seem to be on the verge of learning something fundamental about form, order, and change in the world at large. This is a quest for something far greater than mere technological achievement, which, unfortunately, is the aim and end result of much of the current waste of talent and money in the name of space research. It is a quest for real understanding of the nature of things. Astronomers, using large telescopes on the ground, have already begun to understand the processes of star formation, the subsequent history of stars as they live out their fuel supply,

the formation of the chemical elements, and the connected history of galaxies made up of evolving stars.

It seems to me that any popular book on astronomy must carry part of this story to its readers. A generation ago the minds of the young people who became our present-day astronomers were stirred by the popular books of Jeans and Eddington, such as *The Mysterious Universe*, *The Nature of the Physical World*, *The Expanding Universe*, and *Stars and Atoms*. Unfortunately, no new books of equal caliber are available even though our knowledge of astronomy is much greater today than it was 20 years ago. Currently there is much popular writing aimed at awakening the imagination to the glamor of space-flight technology. But this is not astronomy. Unless basic astronomy is shown to be as exciting as artificial satellites, the young people who are our potential scientists will grow up with a desire to light wicks under rockets rather than to operate 200-inch telescopes.

Although Bok, widely known as one of the most versatile and stimulating teachers of astronomy, has shown his ability as an author in his previous book *The Milky Way* (written with his wife), his present book falls short. It bears the marks of hasty composition and carelessness with regard to details. It leaves a final impression of being principally a collection of facts, often thrown together without underlying direction. Facts in popular writing must be ordered if they are to tell a story. The "plot" seems to be missing. The facts, in themselves, are sometimes interesting, and indeed they are of the sort necessary for a modern synthesis of the universe. But the synthesis is not made.

The first section of the book deals with the atmospheres of the planets, the origin of the solar system, and the nature of the solar atmosphere. A description of the chemical constitution and temperatures of planetary atmospheres is given and the widely accepted conclusion is reached that no other planet

in the solar system is suitable for human life. The theories of the origin of the sun and the solar system are traced from Laplace's nebular hypothesis, through the collision theory of Chamberlain and Moulton, to the revised nebular hypothesis of Von Weizsäcker.

The second chapter, "Stars as individuals," describes distance determinations, the H-R diagram, binary stars, mass determinations, variable stars and novae, and finally defines the two population types of stars. This chapter and the fourth chapter show signs of hasty preparation. In a popular book one certainly cannot insist on precise statements, but correct statements can be expected. For example, Figure 1 on page 27 implies that subdwarfs are population I stars, but there is strong evidence that they are halo objects of population II. Bok also repeats the modern trend that ignores the early Mount Wilson work on spectroscopic parallaxes upon which all the subsequent work in this field has been based. He states that "the techniques of spectral-luminosity classification have been developed especially by Lindblad and his students in Sweden, by Morgan and associates in America, and by Chalonge and his group in Paris." All this is true, but the original discovery of the method and the basis upon which Lindblad and Morgan have built was entirely a Mount Wilson project carried out by Adams and Joy. And in another section the statement is made that "the origin of stellar variability must be sought in the deep interior of the star and the basic cause of the variability lies probably in some imperfect balance of the energy generating processes in the star's interior." This view is not held by most astrophysicists. Rather, all evidence seems to point to a surface instability of the ionization zone of some critical element as the cause of stellar variability.

The third chapter on the Milky Way system is perhaps the best written of the four. Radio astronomy and the 21-centimeter line of hydrogen are described in some detail. The interstellar gas and dust and the current data on the spiral structure of the galaxy are discussed. Here Bok is in his element and the chapter is good.

The fourth and final chapter tells of the newest and, perhaps, most important current trend in astronomical research—the expanding universe, the cosmic time scale, and stellar evolution. Again several points are reported in this chapter which professional astronomers

would like to see more fully explained. For example, the discussion of the cosmic time scale, does not mention the fact that a world model *must be assumed* before an age can be assigned to the expanding universe from our knowledge of the present expansion rate. Furthermore, the most important method of dating stars in our galaxy—the use of H-R diagrams of galactic clusters—is not mentioned. Also, Figure 6 on page 87, which shows the evolution of stars of solar mass, is somewhat misleading because stars of 1.2 masses are very probably not operating on the carbon cycle as shown, but rather generate energy by the proton-proton chain. For this reason, it is quite likely that these stars do not have a convective core. If a convective core were present the characteristic Hertzsprung gap would occur in the diagram. Its absence is a notable feature of the H-R diagram for globular clusters. Finally, it is nowhere mentioned that the track shown in Figure 6 is for a star with very low metal abundance such as the stars in globular clusters. Stars with a normal chemical composition (like the sun) will have evolutionary tracks which differ greatly from the track shown.

Bok's book, although not as detailed or as carefully written as many professional astronomers might wish, should appeal to the lay reader, especially if it is used in conjunction with more comprehensive books such as *The Milky Way* (Bok and Bok) or the other works listed in the extensive bibliography at the end of *The Astronomer's Universe*.

ALLAN SANDAGE

Mount Wilson and Palomar Observatories, Carnegie Institution of Washington, and California Institute of Technology

The Population Ahead. Roy G. Francis, Ed. University of Minnesota Press, Minneapolis, 1958. x + 160 pp. \$3.75.

"Man knows more than he thinks he does," says Roy Francis, the editor of this symposium volume. Unfortunately, it is often difficult to apply what is known to some of the acute social and economic problems confronting the modern world, because a good deal of the existing store of knowledge is not really in the public domain. Though not under security wraps, it is virtually inaccessible because it is presented in the strange jargons of scientific specialization. It may be food for pedantic thought, but

it is not "Gerberized" to titillate the intellectual palate of the layman. Francis' solution for this problem is "the desegregation of knowledge." Such a term, to be sure, is not now current: "in today's lexicon one 'segregates' on the basis of skin color, not of academic hue." The segregation of ideas, by preventing knowledge from being an effective power for reform or reorientation, can be devastating in its effects.

An area gravely befogged by segregated knowledge is that of population dynamics. The human race is in the midst of an explosion of people the like of which has never occurred before. The rate of this explosive increase—1.5 percent a year—would not impress a financier. Yet it means that when next week's edition of *Science* is distributed, there will be nearly a *million* more human beings on this earth than there are today. In the book under review, P. K. Whelpton notes that if the one-third of a billion human beings presumed to have been living at the time of Christ had increased since that time at a mere 1.5 percent a year, the present population of the planet would be more than a million persons per *square foot* of the earth's land surface. Clearly, this far outdoes the mediaeval concern over balancing angels on the head of a pin.

The Population Ahead is a laudable attempt to desegregate knowledge regarding the population question, which is now cooped up behind the conceptual curtain raised by social scientists, economists, nutritionists, demographers, geographers, and anthropologists. In 1957, the University of Minnesota's Center for Continuation Study (a sort of perpetual idea-desegregating apparatus that ranges widely over many domains of knowledge) brought together a panel of experts and *begged* them to talk in plain English to each other and to a participating audience of several hundred. The result was by no means an intellectual Little Rock. Everybody was eager to live and let live, and there was a very free exchange of ideas, but some of the audience may have been on the verge of conceptual anoxemia. The wide range of views presented does throw considerable light on the population problems, even though the focus is not always sharp.

The question which stood out as the theme of the conference was, "What constitutes an optimum population?" Though opinions vary greatly, this is a question which deserves far more thought than it is now getting. Even in most fortunate America, it is by no means an academic question. The idea is abroad

that by 1975 two-thirds of the population of the United States (perhaps 235 million) will be living in the 165 to 170 standard metropolitan areas, and that this will necessarily be a good thing. Well, will it be or not? Is there a more favorable distribution of people, and what might be done to bring about such a distribution in a free society? These are the questions that are not asked, perhaps because nobody wants to look straight at them.

One thing is certain: population is definitely everybody's business, and the most complete desegregation of knowledge is necessary if what man knows about this subject is to be put to work short of disaster. If the population explosion continues at the present rate, something will have to give. And some of the things which will inevitably give, and before very long—in the United States as well as everywhere else—are the level of living and freedom of thought and action and initiative. Ancel Keys is sure that the earth can provide a survival diet for a good many billion people. Before we test that conclusion let us try to reach some decisions regarding the kind of planet we want to live on.

The varied ideas of nine experts, plus the supporting commentary by a somewhat larger chorus, that make up this symposium volume hardly give a microscopically clear image of the problem. But the book contains more than a K-ration of food for thought.

ROBERT C. COOK

Population Reference Bureau, Washington, D.C.

The Earth beneath the Sea. Francis P. Shepard. Johns Hopkins Press, Baltimore, 1959. xii + 275 pp. Illus. \$5.

Francis Shepard's newest book deals with the vast area, three-fifths of the earth's surface, which lies under the sea. He writes in a simple, direct style which requires no specialized vocabulary from the reader, yet he covers salient aspects of all of the basic geologic problems one encounters beneath the sea. Laymen will find this book well worth reading. In it they will find discussion of many things which are readily observable near the sea—coastal erosion and engineering, currents, waves, and coral reefs. The more exotic phenomena, such as submarine mountains and canyons, are treated in an equally readable manner.

Scientists active in marine research

will enjoy the pungent restatement of problems and will appreciate Shepard's treatment, based on long familiarity with marine science. The point of view is stimulating and provocative in many places—for example, in the discussion of the effects of turbidity currents, the origin of continental shelves, and the origin of submarine canyons. Students interested in geology or marine science should read this book carefully for here, in one small volume, are many of the ideas of one of the pioneers and leaders in the field. The book is not a textbook and does not attempt to outline all points of view on specific subjects; yet there is adequate documentation of the views presented.

Shepard is professor of submarine geology at Scripps Institution of Oceanography, University of California. He was one of the first Americans to study marine geology. From the first days of his study of marine science, 35 years ago, he has always been an active field investigator, going out on ships and making studies on the beaches. His book is particularly timely in this era when the American people have suddenly become aware of oceanography as something of crucial importance to national safety and welfare.

JOHN M. ZEIGLER

*Woods Hole Oceanographic Institution,
Woods Hole, Massachusetts*

Primitive Peoples Today. Edward Weyer, Jr. Doubleday, Garden City, N.Y., 1959. 288 pp. Illus. \$10.

Shortly after the mailman brought my review copy of *Primitive Peoples Today*, our 16-year-old baby sitter (for grandchildren) appropriated it. "I could understand every word of it," she said. "It should be in every high school in America." Later on I read it, and I am not sure that it will be in every high school. Weyer has not hesitated to discuss forms of human behavior rarely mentioned in high schools, except in the washroom. But I may be wrong, for I have not been to high school for 40 years, and things may have changed.

Edward Weyer, Jr., has been on archeological and ethnographic field trips in Egypt, in the arctic, and in Mato Grosso, Brazil. He has been a professional photographer and president of the Explorers' Club. He was editor of *Natural History* for 22 years, during which time his magazine contained few articles incomprehensible to a 16-year-old,

though it did contain some magnificent pictures. The success of *Primitive Peoples Today* should surprise no one familiar with the details of Weyer's career.

For some years jumbo books, printed in Switzerland, have been appearing, full of illustrations, particularly in color, but they have dealt primarily with zoology and have borne names such as Bourlière and Sanderson on the title page. Now Weyer has carried this format into anthropology. In appearance, his book compares favorably with the lion and baboon atlases.

Weyer begins with a short introduction, called "The world of primitive man," in which he first defines the objective anthropological viewpoint, with its sliding scale of moral values, and then develops an essentially Boasite attitude toward culture, in which attempts to establish levels of complexity are discouraged. He then discusses the races of man from the same point of view, favoring nurture over nature as a cause of differences in achievement. Blood groups and other hereditary traits are discussed in simple language. He produces the old saw that "between 90 and 99 percent of the approximately 44,000 pairs of genes in each individual are shared by all other groups of men," without saying how many may be shared with apes (which have the same chromosome count that we do), or even with frogs. Again, he says, "a child will look like an Eskimo or Zulu depending entirely on whether he is born one, [but] he will grow up acting like an Eskimo or a Zulu depending on the culture in which he is raised." This is standard Boasism, which bypasses many issues. No Eskimos have been fostered by Zulus, or vice versa.

We move on to a series of cultural vignettes of the Eskimos, Aleuts, Navahos, Lacandonese, San Blas Indians, Jivaros, Camayurás, Lapps, Ovimbundu, Bushmen, Ainus, Lolos, Aruntas, and Samosans, to each of which about six large pages are devoted. In ten instances these vignettes are illustrated by photographs of the tribe under discussion. There are no illustrations of the Aleuts, Ovimbundu, Lolos, and Aruntas. Instead we are shown pictures of 40-odd other peoples.

The vignettes are arranged geographically, without regard to race or cultural connection, and the pictures follow this same pattern. In each vignette a striking feature of the particular culture is emphasized, and often a personal-narrative technique is used. The style is lively, and the people are made to seem alive.

The splendid pictures are reproduced

on pages 8½ by 11 inches, and some are run across two pages. They were taken by 40 different photographers, of whom many are professionals, such as Fritz Goro, Alfred Eisenstaedt, and Eliot Elisofon. Both the black-and-white and the color reproduction are superb. The selection is also excellent in that few of the photographs are static and nearly all show people doing things that are of interest to anthropologists. Even the posed shots of the Ainu "chief" Miyamoto and his group (who have their pictures taken every day) are convincing to those who do not know him. A few illustrations are miscaptioned—for example, number 83, "Tuareg men eating on the desert trail near the Hoggar Mountains. One man has lowered his veil. Popular accounts have overstressed the importance of the veil among Tuareg men. . . ." The man with the lowered veil is no Tuareg, but a slave. The importance of the veil has not been overstressed.

It is hard to figure out exactly what audience this book is intended for. Too spicy, perhaps, for high schools, it is too naive for most anthropologists. However, there is a vast public in this space age which thinks the world is as homogenized as their breakfast milk, that everyone who lives in Russia is a Russian, and that all Africans are Negroes. As painlessly absorbed as a magazine in a barber shop, *Primitive Peoples Today* can show these folk how wrong they are. In this conquest of complacency I wish it luck.

CARLETON S. COON

*University Museum,
University of Pennsylvania*

Vegetation of the Outer Banks of North Carolina. Clair A. Brown. Louisiana State University Press, Baton Rouge, 1959. x + 179 pp. Illus. \$3.

Vegetation of the Outer Banks of North Carolina is the result of a reconnaissance of the area to study the effectiveness of the sand-stabilization projects of the 1930's and to secure information on other sand-binding plants in the native vegetation. A botanical study was also made.

On the outer banks, sand fencing has been effective in establishing barrier dunes. American beach grass, sea oats, salt meadow cord grass, and Bermuda grass are the important grass binders. *Paspalum vaginatum* seems to offer the greatest possibilities among binders not

previously used. The woody species were not as effective as the grasses as sand binders.

The dunes (wooded and grass-covered), sand flats, and salt marshes are described. A list of the vascular species observed is included. The highlights of the report are the 50 illustrations, each 4 by 6 inches; the geographical and historical account is adequate, and there is a fairly complete bibliography pertaining to the vegetation of the area.

As a preliminary survey of the vegetation and as a report on sand-stabilization practices, the book is excellent. The title, however, is misleading in that the listing of 273 species, when there is a possibility that 400 species occur in the area, gives an inadequate picture of the vascular vegetation. The records at the University of North Carolina indicate a flora of at least 850 species. The author indicates (page 87) that "there are many phases of Plant Geography, and Ecology which remain to be unravelled by detailed studies of this interesting area" from a plant-community standpoint.

The figures, history, and geography should make this book of interest to tourists visiting the Cape Hatteras National Seashore Project, but as a scientific presentation, this is a preliminary study only.

ALBERT E. RADFORD

Department of Botany,
University of North Carolina

Progress in the Chemistry of Organic Natural Products. vol. 16. L. Zechmeister, Ed. Springer, Vienna, Austria, 1958. 226 pp. Illus. \$9.50.

In the past this useful series of reviews has been noted for the wide variety of fields it has covered. Almost every conceivable technique or approach capable of yielding information regarding the structure of natural products, how they are made in nature, and their probable function has been touched upon in some way. Since each volume is a collection of relatively short reviews, there is little space for developing the subjects in such a way that anyone who is not a specialist in the particular field and even in the particular techniques used can always fully appreciate them. Perhaps this is inevitable, and the reader should at least be thankful that most of the more recent literature is given in the bibliography, which will serve as a starting point for a more penetrating study. Two of the reviews

in particular in volume 16 appear to fall in this category—namely, the third and the fifth.

The first review, 25 pages in length and written in German by Von Karl Freudenberg and Klaus Weinges, covers a class of naturally occurring phenolic substances—the catechuic acids, hydroxyflavanes, and hydroxyflavones—usually treated as part of a wider field of plant dyes and intermediates. As a class they merit treatment in this way.

The second review (62 pages), by Karel Wiesner and Zdenek Valenta, on the chemistry of the aconite-garrya alkaloids, is an exceptionally timely and interesting one, because much light has been thrown on this complicated group of natural products in recent years by the newer experimental methods such as infrared and x-ray analysis. For relatively small molecules of diterpenoid nature they are amazingly complicated. As the authors point out, a solid basis for the more recent structural conclusions was made mostly by W. A. Jacobs and his collaborators, working along classical lines of organic chemistry. It is only to be expected that the more recent work, with the greatly improved tools for interpreting chemical transformations, would make possible a more enlightened choice of key members of such a large group, but it would still be patterned after the original truly pioneering work. Some of the structures proposed will form the basis for deriving still more complicated structures in this field, while others already seem to be of doubtful validity on the basis of present information.

The third review, ably written by E. E. von Tarnen, suffers from the fact that it attempts to cover too large a field in too short a space. In 24 pages the structures of 24 different types of antibiotics are treated. Even though all are produced by the actinomycetes group of microorganisms, they range widely in structure from highly unsaturated straight-chain fatty acids to complex cyclic polypeptides containing ten amino acids and a heterocyclic nucleus. Since much space is occupied by the accepted structural formulas little is left for discussion of the unique structural features particularly characteristic of these compounds. To be sure, many of them are mentioned but, in my opinion, not with sufficient discussion for such a truly fascinating field. Does the fact that we now have so many new and different structures to consider mean that we are content to know but little of each one? Unlike the fields covered in the first two

reviews, all of the substances considered have been isolated very recently.

The fourth chapter, by James Bonner, covers a field, "Protein synthesis in plants," which is developing so rapidly at the present time that workers not in the field will surely welcome this short review (29 pages) as a means of trying to keep informed. Protein synthesis is certainly one of the most important areas of biochemical research today. This is true in spite of the fact that we are still sadly lacking in knowledge of the detailed structure of proteins and know only the rougher outlines with regard to the structure of the nucleic acids. Since the interdependence of the two classes is now well established, an understanding of both on a molecular level must be achieved.

The final chapter, by Hans Kuhn, deals with the "Electron gas theory of the color of natural and artificial dyes: problems and principles." The first third of the review deals with experimental facts concerning color and structure. This will be of interest to organic chemists working in the field of natural products, but it is doubtful that many will have the background or even the inclination to become sufficiently well versed in quantum mechanics to properly understand the whole treatise. Even though an ultimate and complete understanding of the structure of an organic compound does require an understanding of the structure of each atom, it is seldom practical to try to treat all of such a mass of information in one short article.

Volume 16 of *Progress in the Chemistry of Organic Natural Products* is a worth-while addition to any chemical library.

LYMAN C. CRAIG

Rockefeller Institute

Manual of Insect Morphology. E. Melville DuPorte. Reinhold, New York; Chapman and Hall, London, 1959. xi + 224 pp. Illus. \$5.

The appearance of a manual of insect morphology written by Melville DuPorte, an authority in the field, is an event of the first importance. The arrangement of the book is original and practical, from the viewpoint of the teacher. The idea of beginning each section with general considerations (which in the strict meaning of the term *morphology* is the morphological part of the book; the rest being straight anatomy)

is a good one. In starting with the abdomen of the insect, which is the easiest part to demonstrate and explain to the beginning student, and in taking up the more difficult and complicated parts—the thorax and the head—later, DuPorte gives evidence of long experience as a teacher.

In the introduction DuPorte emphasizes that he is especially interested in the evolution of insects. Even though he does start with generalized forms and moves on to more complex ones, this important phase of the subject seems to be played down.

Undoubtedly DuPorte covers these points completely in his lectures and in the laboratory. Apparently, in his cautious conservatism, he considers such material to be out of place in a laboratory manual for undergraduates. I hope that sometime in the future he will expand this phase of his work, thus providing in his published work the stimulus which a scholar such as he is capable of giving.

F. H. BUTT

Department of Entomology,
Cornell University

Anatomy of the Human Body. R. D. Lockhart, G. F. Hamilton, F. W. Fyfe. Lippincott, Philadelphia, Pa., 1959. ix + 695 pp. Illus. \$13.50.

The drastic reduction which has been made in the amount of time allotted to the teaching of gross anatomy in the curricula of many medical schools in this country has probably been a factor in encouraging both authors and publishers to bring out textbooks for such courses which, though considerably more comprehensive than those designed for non-medical students, are still somewhat briefer than the traditional *Gray*, *Morris*, or *Cunningham*.

This volume by Lockhart, Hamilton, and Fyfe represents the most recent of these attempts to "lighten the burden of the student of anatomy," as these authors define their objective in the first sentence of their preface. It contains 697 pages, as compared with the 1500 to 1700 pages of the larger textbooks of gross anatomy. The reduction in the amount of text, however, cannot be gauged accurately by this comparison, because the use of a somewhat smaller type and of two 3-inch columns per page effects a considerable saving in space. As a result, a full page in this volume contains about one-third more words than

an average page in one of the larger textbooks of anatomy. Since, however, there are more than 125 full-page illustrations in addition to at least twice that number of part-page illustrations of one-half page or more, it is obvious that the authors have achieved a very great reduction in the amount of text material. The illustrations (approximately 950 in number and most of them in color) are, in general, excellent, and their quantity and scope are such that the volume would serve most students quite satisfactorily both as an atlas and as a text.

The section on the nervous system deserves special comment, because of the unique way in which the text and the related illustrations are combined. Many of the illustrations are printed on the same page as that part of the text which pertains to them; indeed, the pertinent text is, in some instances, arranged in irregular columns which conform to the available space between adjacent illustrations. The names of key structures in the text are set in bold-faced type and are connected directly by lines to those parts of the illustration in which the structures are pictured. Thus, verbal description and pictorial representation are brought together in a manner which should be very helpful to the reader.

I am quite aware that it takes rather less wit to pick a few flaws in someone else's work than it does to create something half so meritorious. I hope, however, that at least the first two of the following three minor criticisms will be considered constructive ones, as I intend them to be.

On pages 142 and 143, the authors present a series of outline drawings showing, among other features, the position, age at first appearance, and age at fusion of various secondary centers of ossification. The ages given for some of these—those for the centers of the hand, for example—are not correct. Adequate data on the age at which these skeletal changes occur are now available from a number of radiographic studies of normal living children in Europe and in this country. The authors may wish to consult these data when they prepare the next edition of their book. The relative skeletal precocity of girls as compared with boys would seem, also, to deserve some mention in this connection.

On page 183, in the description of the *rectus abdominis*, the authors define the *linea semilunaris* as delimiting the lateral, convex margin of that muscle. Spieghel originally applied the term *linea semilunaris* to the line of approximately half-moon shape which marks

the border between the muscle fibers and the aponeurosis of the *transversus abdominis* muscle. The *linea semilunaris*, as thus defined, is for the most part situated lateral to the lateral border of the *rectus abdominis* muscle. This is, admittedly, a minor point and one which would not be worth mentioning if one were not commenting on a book in which such a generally high degree of terminological accuracy has been achieved.

One of the authors' expressed intentions in writing this book was to eliminate "such obvious statements as 'the skin covers the body'" and "to modify the rigid formula for relations known to produce such answers as 'the mouth is situated on the face and its anterior aspect externally communicates with the atmosphere.'" They have succeeded admirably in fulfilling this intention, but, in at least one instance, they seem to have slipped. On page 342, in discussing the nerves to the bladder, we find this little gem: "disturbance of micturition (evacuation of the bladder) is of great practical importance." It is reassuring, in these troubled days, to encounter at least one statement upon which there would be unquestioned international agreement—even among anatomists!

The present volume gives evidence of much sound scholarship, a great amount of labor, and considerable ingenuity in devising methods of increasing the effectiveness of illustrations as teaching aids. The book's obvious merits will commend it to medical students, to teachers, and to all others who have occasion to use it.

WILLIAM WALTER GREULICH
Department of Anatomy,
Stanford University School of Medicine

Applications of Finite Groups. J. S. Lomont. Academic Press, New York, 1959. xi + 346 pp. Illus. \$11.

It has been a matter of pride with most physicists to announce that they do not use group theory to obtain their results. Actually, what they do is to replace an organized, logical, and general method by rudimentary "common-sense" methods.

The avoidance of group theory has led to many misleading statements in our textbooks. For example, in most books on quantum mechanics the author starts from the commutation relation for p_1 and q_1 and derives the commutation relations for orbital angular momentum.

Then he "generalizes" these to any angular momentum. Actually, the commutation relations for the total angular momentum of a system are a consequence of the assumption of isotropy of space.

For problems with complicated symmetry properties (molecular vibrations, crystalline fields, nuclear models), the power of the group-theoretical methods has been recognized, and physicists working in these fields have been forced to learn the requisite mathematics.

The use of invariance principles to determine the possible types of elementary systems has only recently become familiar to physicists. E. P. Wigner, in particular, has stressed this approach to fundamental problems. The study of relativistically invariant systems should be based on the properties of the representations of the Lorentz group, and not on a particular differential equation.

Lomont's book is an encyclopedia of theorems concerning finite groups, plus sections enumerating results for the three-dimensional rotation group and the Lorentz group. Very few theorems are proved. The reader who is already familiar with group theory will find many remarkable results quoted, so that the book serves as a valuable guide for finding out what problems have been solved. In this respect the value of the book would have been greatly increased had the source of specific theorems been indicated.

Applications of group theory to molecular vibrations, perturbation theory, atomic structure, and crystal lattices are given. In most cases, the concise presentation would make excessive demands on a reader coming upon the subject for the first time.

MORTON HAMERMESH

Argonne National Laboratory,
Lemont, Illinois

New Books

Absorption and Dispersion of Ultrasonic Waves. Karl F. Herzfeld and Theodore A. Litovitz. Academic Press, New York, 1959. 553 pp. \$14.50.

The Human Integument. Normal and abnormal. A symposium. Publ. No. 54. Stephen Rothman, Ed. AAAS, Washington, D.C., 1959. 270 pp.

Medical Sciences. vol. 2. J. C. Bugher, J. Coursaget, J. F. Loutit, Eds. Pergamon, New York, 1959. 296 pp. \$15. Some of the papers relating to medical sciences from the Second International Conference on the Peaceful Uses of Atomic Energy (1958) are published in this

volume. In his preface Bugher states that the editors have attempted to make the volume representative of the content of the conference. An appendix gives details of the medical sessions.

Molecules and Mental Health. Frederic A. Gibbs, Ed. Published for the Brain Research Foundation by Lippincott, Philadelphia, Pa., 1959. 201 pp. \$4.75.

Pathology of Tumours of the Nervous System. Dorothy S. Russell and L. J. Rubinstein. Arnold, London, 1959. 324 pp. \$13.50.

Physics, an Exact Science. Harvey E. White and Eugene F. Peckman. Van Nostrand, Princeton, N.J., 1959. 518 pp. \$5.96.

Physiology of Prematurity. Transactions of the third conference. Jonathan T. Lanman, Ed. Josiah Macy, Jr. Foundation, New York, 1959. 157 pp. \$3.

The Population of the United States. Donald J. Bogue. With a chapter on "Fertility" by Wilson H. Grabill. Free Press, Glencoe, Ill., 1959. 892 pp. \$17.50.

Poisonous Amphibians and Reptiles. Recognition and bite treatment. Floyd Boys and Hobart M. Smith. Thomas, Springfield, Ill., 1959. 162 pp. \$4.75.

Principles of Geology. James Gilluly, A. C. Waters, A. O. Woodford. Freeman, San Francisco, Calif., ed. 2, 1959. 544 pp. \$7.50.

Pueblo de Arroyo Chaco Canyon, New Mexico. Misc. Collections vol. 138, No. 1. Neil M. Judd. Smithsonian Institution, Washington, D.C., 1959. 230 pp.

Radar Meteorology. Louis J. Battan. Univ. of Chicago Press, Chicago, Ill., 1959. 172 pp. \$6.

Radioisotopes for Industry. Robert S. Rochlin and Warner W. Schultz. Reinhold, New York; Chapman & Hall, London, 1959. 200 pp. \$4.75.

Ramification Theoretic Methods in Algebraic Geometry. Shreeram Abhyankar. Princeton Univ. Press, Princeton, N. J., 1959. 105 pp. \$2.75.

Recent Progress in Hormone Research. Proceedings of the Laurentian Hormone Conference 1958. vol. 15. Gregory Pincus, Ed. Academic Press, New York, 1959. 520 pp. \$12.50.

Seventh Symposium (International) on Combustion. At London and Oxford, 28 August-3 September 1958. Published for the Combustion Institute, by Butterworths, London, 1959. 1005 pp. \$35. Contents: pt. 1, "Mechanism of combustion reactions"; pt. 2, "Spectroscopy of flames"; pt. 3, "Ionization in flames"; pt. 4, "Structure and propagation of flames"; pt. 5, "Ignition and limits of inflammability"; pt. 6, "Interaction of flames and surfaces"; pt. 7, "Turbulence in flames"; pt. 8, "Combustion in practical flowing systems"; pt. 9, "Detonation and its initiation"; pt. 10, "Special fuels"; pt. 11, "Instrumentation in combustion research." There were 254 participants from Great Britain, United States, Germany, France, Belgium, Netherlands, Canada, U.S.S.R., Japan, Spain, Sweden, Africa, Australia, Poland, Hungary, Liechtenstein, Norway, and Yugoslavia.

Simple Methods of Contraception. An assessment of their medical, moral, and

social implications. Winfield Best and Frederick S. Jaffe, Eds. Planned Parenthood Federation of America, New York, 1959. 63 pp.

The Technology of Printed Circuits. The foil technique in electronic production. Paul Eisler. Academic Press, New York, 1959. 415 pp. \$12.

Textbook of Toxicology. Kenneth P. DuBois and E. M. K. Geiling. Oxford Univ. Press, New York, 1959. 313 pp. \$6.50.

Theoretical Organic Chemistry. Papers presented to the Kekule Symposium. Butterworths, London, 1959. 315 pp. \$9.50. The symposium, organized by the Chemical Society on behalf of the Organic Chemistry Section of the International Union of Pure and Applied Chemistry, was held in London, 15-17 September 1958. The 19 papers published in this volume provide the full proceedings of the symposium.

Transplantation of Tissues. Skin, cornea, fat, nerves, teeth, blood vessels, endocrine glands, organs, peritoneum, cancer cells. vol. 2. Lyndon A. Peer, Ed. Williams & Wilkins, Baltimore, Md., 1959. 703 pp. \$20.

Turbulent Transfer in the Lower Atmosphere. C. H. B. Priestley. Univ. of Chicago Press, Chicago, Ill., 1959. 137 pp. \$3.75.

When Negroes March. The march on Washington movement in the organizational politics for FEPC. Herbert Garfinkel. Free Press, Glencoe, Ill., 1959. 224 pp. \$4.

Reprints

Bees. Their vision, chemical senses, and language. Karl von Frisch. Cornell Univ. Press, Ithaca, N.Y., 1958 (reprint of ed. 1, 1950). 128 pp.

Conceptual Thinking. A logical inquiry. Stephan Korner. Dover, New York, 1959 (republication of ed. 1, 1955). 309 pp. \$1.75.

From Euclid to Eddington. A study of conceptions of the external world. Edmund Whittaker. Dover, New York, 1959 (republication of ed. 1). 221 pp. \$1.35.

Experience and Nature. John Dewey. Dover, New York, 1959 (republication of ed. 2). 463 pp. \$1.85.

Philosophy and the Physicists. L. Susan Stebbing. Dover, New York, 1959 (republication of ed. 1, 1937). 311 pp. \$1.65.

The Philosophy of Space and Time (Philosophie der Raum-Zeit-Lehre, 1927). Hans Reichenbach. Translated by Maria Reichenbach and John Freund. Dover, New York, 1957. 311 pp. \$2.

The Primitive World and Its Transformation. Robert Feys. Cornell Univ. Press, Ithaca, N.Y., 1959 (reprint of ed. 1, 1953). 198 pp.

Science and Imagination. Marjorie Nicolson. Cornell Univ. Press, Ithaca, N.Y., 1959. 249 pp.

A Way of Life and Selected Writings of Sir William Osler. 12 July 1849 to 29 December 1919. Dover, New York, 1959 (reprint of *Selected Writings of Sir William Osler*, 1951). 298 pp. \$1.50.

Reports

Occultation of the Bright Star Regulus by Venus

Abstract. This occultation was observed and timed visually early in the afternoon of 7 July, in Madrid, Spain. The duration of the occultation was 11 minutes, 4.4 seconds, and mid-occultation occurred at 14 hours, 25 minutes, 9 seconds U.T. Over 600 individual photographs, which define the relative positions of Venus and Regulus, were obtained.

In this age it is no longer often that astronomers are given the opportunity to observe an astronomical event of significance and beauty for the very first time in recorded history.

The recent occultation of the bright star Regulus by Venus, on 7 July 1959, was such a rare event; there is, indeed, no record of its ever having been observed in the past.

I accordingly resolved to observe this occultation visually and to give my entire attention to watching the phenomenon as closely as possible, not only because this was an "astronomical first" but because no instrumental observation could be expected to cover the entire phenomenon as well as the eye. This was because Regulus was to disappear at the dark, nighttime limb of Venus and to reappear from behind the very bright, daylight limb; the eye is a remarkable instrument for handling such contrasts in brightness, whereas the photoelectric cell, for instance, is relatively helpless.

The occultation of Regulus could not be properly observed in the United States, and so, through the kindness of Donald Menzel, director of the Harvard College

Observatory, who arranged for and directed several "occultation expeditions," and of the National Aeronautics and Space Administration, which gave financial support to the Smithsonian Institution for this venture, I was able to use a 5-inch visual refractor at the Madrid Observatory.

As I watched through the telescope, I kept up a running commentary which was recorded, along with two sets of independent time signals, on two tape recorders. (I had resolved to eliminate nearly all possibility of mechanical or electrical failure. As an additional backup, I also timed the event with a stop watch.)

In Madrid, the occultation occurred in the early afternoon, with Venus high in a bright blue, cloudless sky. For several days in advance, in practice sessions, I had set the telescope on Venus and Regulus separately, but by noon on 7 July, the two objects were already close together in the field, Venus looking like a miniature moon shortly before the first-quarter phase and Regulus like a twinkling bright star against a bright blue background.

It is not customary today in scientific accounts to dwell upon the beauty of a phenomenon. I would leave break with this custom to remark that the moments just before occultation presented a spectacle of singular beauty. If one considers the familiar crescent moon-and-star symbol as represented on a flag or other device, but now replaces it by a miniature, bright yellow, crescent moon with an actively twinkling greenish-yellow star almost within the crescent, and both set as living jewels in a clear turquoise matrix, one will, I hope, pardon my digression. The beauty of the spectacle was further enhanced for me by the knowledge that I was witnessing an extremely rare event, and one which would not again be observed for centuries to come.

Then, suddenly, the actual occultation was at hand.

The visual impression of the immersion was that it occurred very rapidly, and I was rather surprised on the playback of my tapes to find that the period from the time I first definitely noticed

the fading of Regulus to the *g* of *gone* in "it's going, going, it's . . . gone" was 3.2 seconds. In fact, I stated that it seemed to be starting to go 8 seconds before final eclipse, which came at 14 hours, 19 minutes, 37.1 seconds U.T., more than a minute before the published expected time, but this early indication may have been an effect of seeing.

Regulus definitely became enlarged just before it disappeared. The phenomenon looked like a very speeded-up sunset, Regulus disappearing like a drop of greenish liquid coming in contact with an absorbent surface. The greenish hue was very probably a contrast effect between the B-type Regulus and the G-type Venus, even though Regulus was occulted by the dark limb of Venus. The 3-second major phase of disappearance was uniform, or "straight line" as far as my eye could tell.

As reappearance became due, I made it a point to repeat positively that I didn't see it. I first noted the reappearance of Regulus as a tiny yellowish pimple of light, quite attached to the lighted limb of Venus, at 14:30:41.5 U.T. I was rather surprised that Regulus did not appear green by contrast with Venus. The emersion seemed definitely more leisurely than the immersion. Upon playback of the tapes I noted that I said it was still "emerging, emerging, . . ." 12 to 14 seconds after I first saw it. It did not appear to "blossom out" from the lighted limb as it had "blossomed down" at the dark limb. This must probably be ascribed to the great difference in contrast between Regulus and the dark and lighted limbs of Venus, although it must be remembered that the daylight and night upper atmospheres of slowly rotating Venus may not affect transiting starlight in the same manner.

Duration of the occultation in Madrid was 11 minutes 4.4 seconds by both time signal systems recorded by my tapes, but 11 minutes, 4.6 seconds by stop watch. Mid-occultation for Madrid was at 14:25:09.3 U.T. if no correction is made for the fact that the eye will note a star's disappearance before it is photoelectrically invisible and will not note its reappearance until enough light is present to call attention to it. These effects tend to cancel out, although reappearance will probably be noted systematically later than the disappearance point is noted earlier than it actually happened. Reaction time, however, will act in the same sense in both cases, both events being timed later than they really are. Thus 14:25:9 might be adopted for mid-occultation at Madrid.

The effect of irradiation was pronounced. The illuminated hemisphere of Venus looked much larger than the dark hemisphere proved to be; it seemed as

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should not repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to one 2-column figure (that is, a figure whose width equals two columns of text) or to one 2-column table or to two 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].

though Regulus was shining through the dark limb of Venus, if one judged the size of the dark side from the apparent size of the brightness of the luminous hemisphere. This, of course, is a very well-known phenomenon.

Roger Hosfeld, a member of my party, using one of the Madrid Observatory telescopes through the kindness of the director, R. Carrasco, was able to obtain a long series of photographs from which the changing relative positions of Venus and Regulus (with corresponding times) can be obtained. The timing of this occultation serves as an important reference point in the theory of the orbital motion of Venus.

J. ALLEN HYNK

Astrophysical Observatory, Smithsonian Institution, Cambridge, Massachusetts

4 August 1959

Paleolithic Paint

Abstract. Discovery of hematite and kaolinite in excavations of late paleolithic occupation sites at Les Eyzies (Dordogne), France, raises anew the question of the nature of the paint used by paleolithic people. Hematite as a pigment source is widely documented, but the presence of kaolinite imported into prehistoric sites poses problems. The suggestion is made that white clay might have been used as an "extender pigment" to mix with colors such as that derived from hematite.

Archeologic excavations under the direction of H. L. Movius Jr., exposed late paleolithic occupation levels in the Abri Pataud at Les Eyzies (Dordogne), France, during the summer of 1958 (1). Several thousand stone and bone implements, much animal bone, and some human skeletal material was found. In addition, some carving on stone came from the Périgordian Final level and some rock which may have been painted was found in this level as well as in the overlying Proto-Magdalenian level. We are here concerned with the discovery of earth materials which may have formed part of a paleolithic paint palette.

Examples of what the archeologist terms "red ochre" were found in each of the two main cultural horizons. These are small, earthy chunks 2 to 3 cm in maximum dimension. Field examination showed them to be hematite (Fe_2O_3), and x-ray analysis of one showed the hematite to be essentially pure. The chunks had been "used," for each was artificially shaped by abrasion which produced relatively flat, intersecting facets. Similar objects were reported earlier from the nearby Grotte de Font-

de-Gaume and other sites (2). The abrasion is recorded in fine, nearly parallel scratches on the flattened faces. These marks are absent along the narrow ridges separating the abraded faces.

No earthy hematite occurs in the limestone cliffs near the abri, or in the stream deposits of the neighboring Vézère River. Such hematite does occur however, in association with clays of Tertiary age described below.

That the hematite was used as a pigment source is an unproved but not unwarranted suggestion and has been advanced by others for similar finds (2, 3). We are, however, on more tenuous, albeit more tantalizing grounds, when we consider the significance of fist-sized lumps of unctious clay found in deposits of Périgordian Final age of the Abri Pataud. This material is not characteristic of the limestone rubble fill of the shelter, nor is there any known occurrence of pockets of such material in the Cretaceous limestone in which the abri has formed. X-ray analysis shows the material to be the clay mineral kaolinite, a material that could only have been brought into the site by man from some outside source.

Several occurrences of clay are known in the general vicinity of the site, and at least two of these are commercially exploited today. These clays represent the weathering, during the Tertiary, of Cretaceous limestone. They occur in large masses, perhaps in sinkholes, in the uplands flanking the Vézère River valley where the site is situated. Brindley and Comer (4) report both kaolinite and halloysite clays from the Les Eyzies deposits, and x-ray examination of samples I collected reveals the same assemblage.

Why was the clay imported into the abri? It was clearly not for use in pottery making, a technical art which then lay several thousand years in the future. Could it have been used by a local artist? For instance, modeling in clay is known from the paleolithic stations of Tuc d'Audoubert and Montespan (Ariège), France. No clay modeling, however, has yet been reported from the Abri Pataud.

Is it possible that the clay was in some way connected with painting? If so, then it might have been used as a white pigment. White is rare in the surviving paleolithic art of western Europe, although it has been suggested that kaolinite was used as a white pigment in some of the later European paintings (5) and in the prehistoric paintings of Africa (6; 7, p. 250).

Another possibility exists, namely, that the kaolinite was used to mix with colored pigments. Thus the kaolinite could have been used for what is known in the

paint industry as an "extending pigment." An extending pigment should have a low opacity, and the index of refraction of kaolinite (1.560 to 1.570) allows it to meet this requirement. In fact, kaolinite has been used as an extending pigment in modern paint manufacture.

As far as I know, the nature of the vehicle for paleolithic paint is still unknown. It is most generally held that pigments were mixed with animal fats (3, 8). No analyses are available to test this or any other hypothesis. There is some ethnographic evidence, however, that Bushmen used animal fat (7, p. 251; 9) as well as the latex-like sap of some plants (9) as a vehicle for pigment, and urine, milk, blood, and honey also have been suggested (9). Strangely enough, common water has not been suggested as a vehicle.

We do not know whether the occupants of the Abri Pataud used clay in painting. Nevertheless, the presence of clay in the cultural horizons of the abri reminds us that as yet we know very little concerning the technical side of prehistoric painting. We are quite obviously in need of organic and inorganic chemical analyses as well as mineralogical analyses of paleolithic paint.

SHELDON JUDSON

Department of Geology, Princeton University, Princeton, New Jersey

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17 July 1959

Left-to-Right Shunt Detection by an Intravascular Electrode with Hydrogen as an Indicator

Abstract. Hydrogen gas crosses the pulmonary membrane and dissolves in blood, and it therefore appears immediately and in high concentration in the left heart and later and in lower concentration in the right heart. The hydrogen-sensing, platinum black-tipped catheter is uniquely sensitive in detecting the left-to-right shunts.

An electrode sensitive to a foreign gas in aqueous solution should have several applications in biological and medical research. The classic hydrogen reference electrode principle has been applied to measure gaseous hydrogen concentration (pH_2), instead of hydrogen ion activity, according to the equation:



Preliminary studies (1) have indicated that, contrary to what might be expected on the basis of the sensitivity of colloidal platinum to "poisoning," a platinum black electrode produces very sizable potentials, with respect to a reference electrode, when exposed to blood containing hydrogen. Potentials of up to 300 mv are observed, and these are, of course, relatively simple to measure and record even in the presence of the potentials generated by the heart.

A number of types of platinum and palladium electrodes were prepared and tested. Platinum black electrodes were found to be satisfactory. They were prepared by making the platinum the cathode (1.5 v) in a 5-percent solution of platinum chloride while using a platinum electrode of similar area as an anode until a perceptibly grey coating was deposited. They retained their sensitivity to hydrogen over a period of several weeks even though allowed to become dry, repeatedly exposed to blood, cleaned, and sterilized by soaking in 70-percent alcohol or by autoclaving. The most convenient reference electrode was found to be a silver chloride coated silver plate cut in the shape of an "L" with the parts long enough to prevent the generation of abnormal reference potentials by fluids contacting a solder joint. This silver-silver-chloride reference was brought into contact with the skin through a saline-soaked pad. Measurements of potential were obtained by connecting the reference and platinum directly to a model G Beckman pH meter, to a 100-mv-span model G-11A Varian, or to a multichannel Electronics for Medicine recording oscilloscope, using any of the d-c amplifier circuits available with this instrument.

A membrane electrode, similar in principle of design to that described by Clark (2), was used to give a signal when hydrogen gas flowed by its tip. In a dog,

one platinum black-tipped catheter was placed in the aorta just distal to the aortic valve; the other was placed in the superior vena cava near the right auricle. The membrane electrode was placed in a tracheal window. Figure 1 is a simultaneous recording of the potentials developed by these electrodes following one breath of 100-percent hydrogen.

The subject for the observation shown in Fig. 2 was a child known to have a pulmonary valvular stenosis and a ventricular septal defect and a predominant left-to-right shunt. Curves *RV* and *IVC* were obtained by moving the electrode-tipped catheter from one location to another, with an inspiration of hydrogen at each location, as described in the

legend. The 2-second-delay fast-slope curve obtained for the right ventricle demonstrates the existence of the left-to-right shunt (subsequently established by blood oxygen analysis and cineangiography).

Although the potential developed by the platinum black-tipped catheters used is not strictly quantitative, the differences in timing, rate of response and final potential developed are so great that little difficulty is encountered in distinguishing between left heart blood and right heart blood after inspiration of hydrogen.

The application of this technique in the detection of left-to-right shunts is being explored in a variety of patients. We are attempting to design a multiple elec-

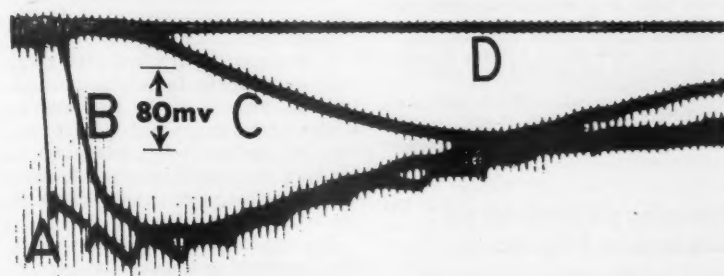


Fig. 1. Potentials developed by tracheal, aortic, and vena caval platinum black electrodes in an anesthetized dog. (A) Trachea. This potential signals the appearance of hydrogen in the trachea. Note also the changes in hydrogen concentration in the trachea as the lungs are cleared of hydrogen by respiration. (B) The increase in hydrogen content of blood in the aorta begins 2 seconds after passage of hydrogen through the trachea is detected. Maximum response occurs in approximately 12 seconds. (C) Increase in hydrogen in the vena cava begins about 8 seconds after hydrogen appears in the aorta and reaches a maximum in about 1 minute. At higher paper speed, the pattern of the electrocardiogram is useful in locating the position of the catheter tip. (D) Base line. Vertical marks are 1-second intervals.

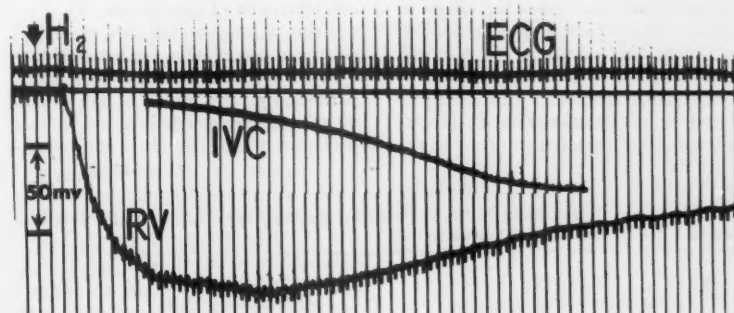


Fig. 2. Hydrogen potentials from right ventricle and vena cava of a patient with a ventricular septal defect and pulmonic stenosis, having a left-to-right shunt. At the point indicated by the large arrow, one breath of hydrogen was administered by mask. The sudden increase in potential from the catheter tip in the right ventricle (curve *RV*) indicates the presence of left heart blood flowing directly into the right ventricle. The superimposed curve (*IVC*) was obtained later from the same catheter after the tip was withdrawn to the inferior vena cava and a second breath of hydrogen was given. The large arrow also indicates the hydrogen inhalation point for the *IVC* curve. The vertical lines show 1-second intervals. Note that the electrocardiogram (*ECG*) is superimposed on the *RV* curve but is barely detectable on the *IVC* curve. Note also the lack of effect of one breath of hydrogen on the electrocardiogram.

trode catheter whereby hydrogen potential measurements may be made simultaneously at various points and where blood samples and pressure measurements can be taken at the same time (3).

LELAND C. CLARK, JR.

L. M. BARGERON, JR.

Departments of Surgery and Pediatrics,
University of Alabama Medical Center,
Birmingham

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Note added in proof: Since this report was submitted for publication, a large number of diagnostic catheterizations have been completed, by means of the hydrogen electrode catheter; these are described in a report in *Surgery* (in press).

13 April 1959

Potentialiation of Epinephrine and Norepinephrine by Iproniazid

Abstract. The effects of pretreatment with iproniazid on the toxicity and cataract-producing ability of epinephrine and norepinephrine were studied. The epinephrine and norepinephrine were administered in such a way that a slow, prolonged rate of absorption was achieved. Under these conditions, the lethality and cataract-producing ability of these amines were shown to be significantly enhanced by the action of iproniazid.

To explain the psychic effects of iproniazid, it has been postulated that this substance potentiates the effects of certain physiological amines by inhibiting monamine oxidase (1). Although potentiation of serotonin (2) and dihydroxyphenylalanine (3) has been produced by preadministration of iproniazid, significant potentiation of the effects

of epinephrine and norepinephrine by iproniazid has not been shown previously.

To demonstrate potentiation by iproniazid, a slow, prolonged rate of absorption of epinephrine and norepinephrine was attained in three ways: by subcutaneous administration, by repeated intraperitoneal injection, and by slow intravenous perfusion of the amines. At more rapid rates of absorption, no potentiation could be shown. For example, we were not able to show potentiation of single intraperitoneal doses of norepinephrine by iproniazid in rats, nor were we able to show a significant difference in the amount of norepinephrine required to kill rats perfused intravenously at a relatively rapid rate.

In the experiments described below, doses of iproniazid reported to inhibit completely monamine oxidase were used (4). Mice routinely received 100 mg/kg, and rats, 50 mg/kg. In each case, enough time was allowed for the iproniazid to inhibit the monamine oxidase before the catechol amines were administered. Doubling the dose of iproniazid in mice did not further potentiate the effects of the amines.

The results given in Table 1 show that iproniazid potentiates the toxicity and cataract-producing ability of subcutaneously administered epinephrine and norepinephrine. Both multiple small doses and a single larger dose of these amines were effective in demonstrating the potentiation. Griesemer had found incidentally that a single subcutaneous dose of 0.5 mg of epinephrine per kilogram which killed none of 15 controls, killed 21 of 41 rabbits that had been injected with 50 mg of iproniazid per kilogram 12 hours and 2 hours prior to the administration of epinephrine (5).

Using a total of 130 rats, we could show no potentiation by iproniazid of epinephrine given in single doses intraperitoneally. The results of the studies of subcutaneously administered amines prompted us to administer the norepi-

nephrine in divided doses intraperitoneally to obtain a more prolonged rate of absorption. One-half milligram of norepinephrine was given every 15 minutes for 13 doses to rats pretreated with iproniazid and to control rats pretreated with saline. Thirteen of 20 rats pretreated with iproniazid and four of 20 controls died of this treatment ($p < 0.01$).

In the studies in which the catechol amines were administered subcutaneously and intraperitoneally, the potentiation by iproniazid could have been due to the fact that the iproniazid prevented the amines from being destroyed before they were absorbed from the injection site. To test this possibility, the amines were infused intravenously at a slow rate. Unanesthetized rats were used, to avoid the effect of drugs which depress the central nervous system, which have been shown to antagonize the toxicity of epinephrine (6). The jugular veins of the rats were cannulated under light ether anesthesia, and an hour was allowed for complete recovery from the anesthetic. The weights of the animals in the two groups were identical. The animals were perfused with DL-norepinephrine bitartrate at a rate of 1 mg/cm³ per 85 minutes. The rats pretreated with iproniazid died after having received 0.73 ± 0.66 mg, the controls, after having received 4.66 ± 1.74 mg ($p < 0.01$). The heightened sensitivity of rats pretreated with iproniazid to intravenously administered norepinephrine indicates that the potentiation seen in the studies in which the amines were administered subcutaneously and intraperitoneally was not due solely to a difference in the amount of intact amine available for absorption.

Seven controls and seven rats pretreated with iproniazid, when perfused with 1.5 mg of DL-norepinephrine per cubic centimeter per 85 minutes failed to show a significant difference in response, although, on the average, less of the amine was needed to kill the animals pretreated with iproniazid (0.83 ± 0.44 mg, as opposed to 2.0 ± 1.33 mg).

It has been shown that iproniazid profoundly alters the metabolism of epinephrine and norepinephrine, presumably by inhibiting monamine oxidase (7). Such inhibition provides a possible explanation for the potentiation of these catechol amines by iproniazid. It may be that the amines must be absorbed slowly in order to show the potentiation because the monamine oxidase system slowly deaminates the amines in vivo, as it does in vitro (8). At faster rates of absorption the monamine oxidase system may have little opportunity to inactivate any of the dose administered before a toxic level is reached; therefore, control animals and animals pre-

Table 1. Effects of iproniazid on the incidence of mortality and of cataract produced by catechol amines given subcutaneously.

Drug and No. of doses*	Total dose (mg/kg)	Species	No. dead at 24 hours per No. used		No. with cataract per No. of survivors at 4 hours	
			Animals pretreated with iproniazid	Controls	Animals pretreated with iproniazid	Controls
Epinephrine, 4	8	Mouse	17/20	5/20 †	7/8	5/17 ‡
Epinephrine, 6	6	Rat	18/18	9/18 †	4/6	0/16 ‡
Norepinephrine, 5	20	Rat	5/8	0/8 ‡	5/8	0/8 ‡
Norepinephrine, 1	12.5	Rat	10/10	4/10 ‡		

* Interval between doses, ½ hour. † $p < 0.01$. ‡ $p < 0.05$.

treated with iproniazid respond similarly.

There is some evidence to indicate that the lethal effects of epinephrine are mediated in the central nervous system, at least in part (9). Penetration into the hypothalamus (10), as a result of prolonged high levels in blood, and subsequent potentiation of the amines centrally is also a possible explanation.

These results tend to support the hypothesis that iproniazid may, in part, exert its effects by potentiating epinephrine and norepinephrine (11).

J. L. BOROWITZ
WILLIAM C. NORTH

Pharmacology Department,
Northwestern University Medical School,
Chicago, Illinois

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25 May 1959

Acrylamide Gel as a Supporting Medium for Zone Electrophoresis

Abstract. Acrylamide polymerized in buffer solutions forms a stable, flexible, transparent gel which is useful in zone electrophoresis.

Many different forms of stabilizing media have been proposed for use in "zone electrophoresis." Since Smithies described the starch gel technique (1), the use of gelling agents to stabilize the migration medium has received increasing attention (2). This report describes a new, commercially available, synthetic gelling agent which has many advantages over previously described agents for electrophoresis.

Cyanogum 41 is a product of American Cyanamid Co. The following paragraph is quoted from the technical information supplied by the manufacturer: "Cyanogum 41 Gelling Agent is a mix-

ture of two organic monomers—acrylamide and N,N'-methylenebisacrylamide—in proportions which produce stiff gels from dilute aqueous solutions when properly catalyzed. The process by which the gels are formed is a polymerization-cross-linking reaction."

Gels can be formed with various buffers according to the directions supplied with the material. The precaution must be observed of covering the surface of the solution so as to exclude oxygen when casting thin sheets or films of the gel. This is easily accomplished by floating a sheet of nonwettable plastic on the surface of the monomer solution during the polymerization period.

We have found that 3- to 5-percent Cyanogum in acid or alkaline buffers (0.3 to 0.01M) produces a satisfactory gel for use in electrophoresis. The gel is optically clear and colorless. The optical density of a 5-percent gel 1 mm thick increases slowly from <0.01 at 650 mμ to 0.04 at 325 mμ, rising sharply between 300 mμ and a peak at about 260 mμ (optical density, 0.41), then rising to an end absorption. The gel is flexible and elastic, stable, and completely insoluble in water, once it has formed. At concentrations of 5 percent and more it is strong enough to support its own weight but is somewhat brittle unless a plasticizer, such as glycerol (5 percent) is included in the formulation.

The rate of migration of serum albumin in 0.1M tris buffer of pH 9, gelled with 5-percent Cyanogum, is approximately 1.2 cm/hr at a field strength of 10 volt/cm. A serum pattern can be developed in this medium in 8 hours, fixed in dilute acetic acid, and stained with bromphenol blue, as in any of the current standard procedures. Washing in dilute acetic acid turns the gel (which takes up the stain) a pale yellow and leaves the protein pattern dark blue. The pattern is sharper than in other commonly used media. Several of the globulin zones are separated into subcomponents.

Hemoglobin in the same medium migrates at approximately one-half the rate of serum albumin. There is less tailing of the hemoglobin bands than is seen on paper strips. There is a marked decrease in the width of individual bands as compared with starch gel patterns. The hemoglobin patterns resemble those seen on agar gel, with some improvement in resolving power. The clarity of the Cyanogum gel permits direct measurement of the pattern by transmitted-light photometry through the gel, without staining.

A particularly convenient way of preserving the electrophoretic patterns, whether stained or not, is to allow the gel to dry out completely. In drying the gel shrinks uniformly in all dimensions,

producing a thin, flexible, transparent, celluloid-like film which preserves the original pattern relationships. This film can be rehydrated to its original dimensions by soaking in water.

SAMUEL RAYMOND
LEWIS WEINTRAUB*

Pepper Laboratory, University
of Pennsylvania, Philadelphia

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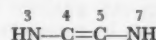
* Present address: University Hospital, Ann Arbor, Mich.

21 May 1959

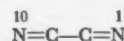
Mechanism of Enzymatic Oxidation of Purines

Abstract. Tautomeric forms of 2-hydroxypurine, in which the structure has been fixed by introduction of an N-methyl group, are oxidized differently by xanthine oxidase. The 1-methyl derivative is attacked at position 8 and the 3-methyl derivative at carbon atom 6. These observations indicate that 2-hydroxypurine itself reacts in a tautomeric form, corresponding to the structure of its 1-methyl derivative.

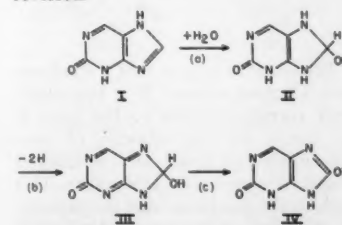
The fact that 2-hydroxypurine (I) is converted by mammalian xanthine oxidase (XO) into 2,8-dihydroxypurine (IV) has been interpreted previously in the following way (1): (a) structure I adds a molecule of water across the CH=N double bond of the imidazole ring; (b) the hydrated form (II) transfers two hydrogen atoms from its central portion, comprising



directly to the corresponding dienic system of the flavin nucleus in xanthine oxidase, represented by the grouping



(c) the intermediate III undergoes a hydride shift to give IV. In this scheme, the order of steps (i) and (ii) may be reversed.



Recent experiments on the enzymatic oxidation of 8-azapurines (2) and pteridines (3), however, make the above interpretation improbable and require a new approach to the mechanistic prob-

Table 1. Physical properties of 2-hydroxypurine and its derivatives.

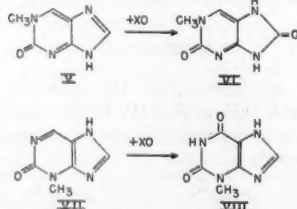
Substance	$\lambda_{\text{max.}}$ at pH 8.0 (m μ)	R_f^* acid basic solvent		Fluores- cence†	Relative rate of oxidation‡ (xanthine = 100)
2-Hydroxypurine (4)	314	0.27	0.24	Blue	16.0
2,8-Dihydroxypurine (4)	304	0.28	0.28	Blue-violet	0.2
1,2-Dihydro-1-methyl-2-oxopurine (V)	318	0.36	0.30	Blue	180.0
1,2-Dihydro-1-methyl-2-oxo-8-hydroxypurine (5)	311	0.34	0.38	Sky-blue	Not attacked
2,3-Dihydro-2-oxo-3-methylpurine (VII)	315	0.51	0.39	Blue	100.0
2,3-Dihydro-2-oxo-3-methyl-8-hydroxypurine (5)	320	0.43	0.42	Blue	2.1
3-Methylxanthine	272	0.43	0.45	Black-violet	Not attacked

* Descending method; the following solvents were used for development: Acid solvent: 95 percent ethanol, 85 ml; glacial acetic acid, 5 ml; water, 10 ml. Basic solvent: 95 percent ethanol, 70 ml; pyridine, 20 ml; water, 10 ml.

† Fluorescence was observed with the aid of a Mineralight ultraviolet lamp, which emits light of λ about 255 m μ .

‡ All substrates were used at a concentration of 6 to 7 $\times 10^{-5}M$.

lem of purine oxidation in general. In order to determine the "active" form of a substrate entering into reaction with the prosthetic group of the enzyme, we have examined two isomeric monomethyl derivatives of I, in which a single tautomeric structure of the latter has become fixed. It was found that 1,2-dihydro-1-methyl-2-oxopurine (V) is oxidized in position 8 and thus resembles I. On the other hand, 2,3-dihydro-2-oxo-3-methylpurine (VII) is converted by xanthine oxidase into 3-methylxanthine. In both cases, identification of the oxidation product was facilitated by the fact that the enzymatic reaction does not proceed beyond the first step. Comparison of the accumulating end products with synthetic materials by paper chromatography and ultraviolet absorption spectra establishes their identity beyond doubt (see Table 1).



These results suggest that I combines with xanthine oxidase in a tautomeric form, corresponding to V. The latter is the fastest reacting substrate of xanthine oxidase yet found, for it is attacked almost twice as rapidly as xanthine. This leads to the conclusion that the pathway of oxidation of purines is determined not so much by the intrinsic polarity of a substrate as by the polarity of the specific enzyme-substrate complex. The active surface may attract preferentially a single structure out of a mixture of

tautomeric forms, thereby inducing a shift in the tautomeric equilibrium of the substrate. This could provide an explanation of the fact that the rate of oxidation of I is only about one-tenth of the rate of V.

HANNA KWIETNY
GERSHON LEVIN
FELIX BERGMANN

Department of Pharmacology, Hebrew University-Hadassah Medical School, Jerusalem, Israel

D. J. BROWN

Department of Medical Chemistry, Australian National University, Canberra

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24 April 1959

Development of Communication between Young Rhesus Monkeys

Abstract. A communication situation is described in which the rewards of both members of a pair of monkeys cannot exceed chance levels unless the operator monkey responds to cues provided by the informant monkey which indicate the location of food. Performance under these test conditions improved progressively to levels consistently above chance.

Although field studies show that communication is of fundamental importance in the organization and control of non-human primate societies, there have been no experimental demonstrations of communication of specific information

between monkeys. This report describes an apparatus for the investigation of communication and presents the results obtained in a preliminary experiment (1). The test situation, shown schematically in Fig. 1, consisted of two barred restraining cages separated by a table. Four pairs of food carts were mounted on fixed runways on the table, and each pair of carts was connected by an expandable rack so that movement of one cart simultaneously extended the other in the opposite direction. Brass handles were attached to each pair of carts on the operator's side, and all carts were equipped with metal food containers which prevented the operator monkey from seeing the food but permitted the partner (informant) to see it.

Before a trial, both opaque screens and the transparent screen in front of the operator were lowered, the food containers of the appropriate pair of carts were baited, and the one-way vision screen was lowered. The trial was initiated by raising both opaque screens simultaneously and by raising the transparent screen in front of the operator 5 seconds later. (The transparent screen on the informant's side was not used in this experiment.) The operator was permitted only one response per trial (non-correction procedure), and after this response the operator's choice and the position of the informant prior to the response were recorded. All pairs were tested twice a day, in the morning and the afternoon, and received 24 trials in each test session. The location of the reward varied randomly, with the restriction that each pair of carts was baited with equal frequency in every block of 24 trials.

The subjects were six pairs of rhesus monkeys, approximately 18 months old, born in the laboratory and removed from the mother at birth. All animals had had previous experience in the apparatus in a series of food-sharing tests in which the food was visible to the subjects and in which all responses by the operator were equally rewarded. For communication testing, one member of each pair was arbitrarily designated the operator, and each pair was given a total of 480 training trials (phase 1). At the conclusion of phase 1, the operator and informant roles were reversed and each pair received 1440 trials under the reversed-role condition (phase 2). Upon completion of this phase of the experiment, the subjects were given an additional 480 trials in the original roles (phase 3).

The results for each phase of the experiment are presented in Fig. 2. The data on the informant's position, the only direct measure of informant behavior obtained in the present experiment, are included for purposes of com-

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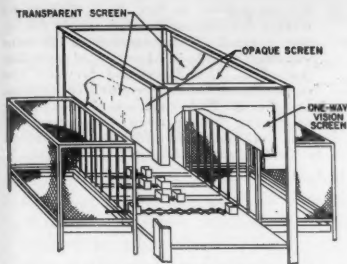


Fig. 1. Schematic drawing of the communication test apparatus.

parison. The analysis, however, is restricted to the performance of the operators. There is no evidence of learning during phase 1, and the percentage of correct responses for individual pairs on the last 5 days of this training period ranged from 23 to 31. Performance during phase 2 improved progressively for all pairs, and this effect of practice is significant at the .001 level as determined by the Friedman nonparametric analysis of variance. Three pairs had two or more errorless sessions during the last half of this phase. To check on possible utilization of nonsocial cues, each operator was given 48 control trials between sessions 46 and 47 of phase 2 in which procedures were identical in all respects to those observed during the regular communication tests except that the informant was not present. For every operator, performance dropped to chance levels.

The differences between performance levels for phase 1 and for the first 10 days of phase 2 were not statistically significant, indicating that efficiency under the reversed-role condition was not initially superior to that demonstrated during the previous phase. Phase 3, in which the monkeys were returned to their original roles, may be regarded as a test of transfer across roles. During the intensive training given in phase 2, each pair achieved performance levels substantially above chance. It might be

expected that in the course of this training the subjects had acquired incidentally some proficiency in the complementary role and if so, that this would be reflected in a high initial level of correct responses on return to the original role. As can be seen from Fig. 2, however, a comparison of data for phases 1 and 3 provides little evidence to support this expectation. Although there is some indication that performance improved during the final five days of phase 3, this effect was not statistically significant and can safely be attributed to practice in the specific role rather than to incidental learning in the course of the previous role.

WILLIAM A. MASON*

Psychology Department,
University of Wisconsin, Madison

Notes

1. I wish to acknowledge the assistance of Jess W. Harris in the design and construction of the apparatus. Support for this research was provided by funds received from the Graduate School of the University of Wisconsin, grant G6194 from the National Science Foundation, and grant M-722 from the National Institutes of Health.

* Present address: Yerkes Laboratories of Primate Biology, Orange Park, Fla.

13 May 1959

Average Potassium Concentration of the Human Body as a Function of Age

Abstract. Potassium-40 measurements on 1590 males and females ranging in age from less than 1 year to 79 years show sex differences and age trends in the ratio of muscle mass to the mass of other body constituents. A sex difference first appears at approximately 12 years of age. While females show a continuous decrease in potassium concentration, males show a rapid increase between the ages of 14 and 16. During adult life both sexes show a persistent and parallel decrease, which may be related to physiologic aging.

In previous papers (1, 2) we reported some of the results of our in vivo measurements of total potassium content of the human body. Measurements were made by counting the gamma rays from natural potassium-40, with a 4 π liquid scintillation gamma counter (2, 3). We now report the results of an analysis of data for 1590 individuals ranging in age from less than 1 year to 79 years. Figure 1 shows the average body potassium concentration (in grams per kilogram of gross body weight) of males and females, plotted as a function of chronological age. The curves show a surprising amount of structure.

Potassium concentration in both males and females increases from the first year of life and reaches a maximum at age 8 or 9, followed by a sharp decline. The

curves for males and females show no significant sex differentiation until approximately the age of puberty (11 to 12 years) in the female. In this age range differentiation begins to occur, and the potassium concentration in females continues to drop rapidly until about age 16 (at which time it assumes a slope characteristic of adult females). Potassium concentration in males shows another sharp increase beginning at age 14 (the age of male puberty) and reaches a second maximum at age 16. The female does not show the second peak at all, and the sex difference is greatest at this age. After the second maximum, potassium concentration in males shows a rapid decline to about age 21 (comparable to that seen in females between the ages of 12 and 16). Beyond age 16 in females and age 21 in males, there is a persistent decrease in potassium concentration with age, with parallel slopes throughout adult life. While the adult decline is shown here as a linear function of age, the data are equally compatible with an exponential decrease.

A statistical analysis of the data for each age group was performed to determine the standard deviation. Since the frequency distribution curves appear to be normal, the precision of the mean for each age group was estimated by dividing the standard deviation by the square root of the number of subjects in the group. The standard deviation of a single datum in the age range from 5 to 68 years (4) was 7 to 15 percent. The standard deviation of the mean for the same age groups was from 1 to 4 percent. The observed scatter of the averaged points about the regression lines is consistent with this degree of precision. The principal cause of variability is the normal biological variation (due largely to difference in amount of fat) among individuals. By contrast, the statistical counting error for each determination was only about 3 percent.

Change in potassium concentration in males and females in relation to growth [as indicated by weight gain (5)] is shown in Fig. 2. Since about 98 percent of body potassium is intracellular (6), change in potassium concentration reflects a change in the ratio of lean, oxidizing, protoplasmic mass to the mass of other body constituents containing little or no potassium (for example, skeleton and fat). The rise in potassium concentration in early childhood reflects increasing muscular development of similar magnitude in both sexes. The decline that begins at about 9 years of age may result, at least in part, from the rapid acceleration in skeletal growth [this is responsible also for the increase in strontium-90 uptake that begins at about this age (7)]. Although growth rate in the female is at a maximum be-

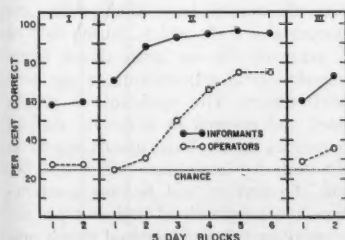


Fig. 2. Percentage of correct responses by the operator and correct positionings by the informant during the three phases of the experiment. Each pair was given 240 trials in every block of 5 days.

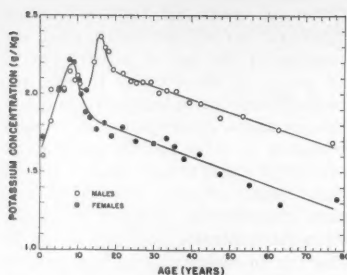


Fig. 1. Average body potassium concentrations of males and females as a function of chronologic age (grams per kilogram of gross body weight).

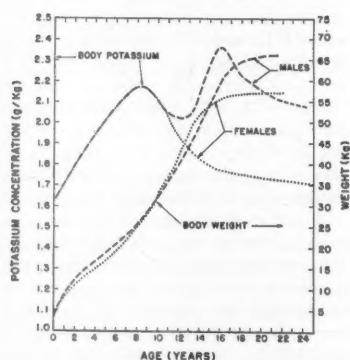


Fig. 2. Change in male and female potassium concentrations in relation to growth (as indicated by weight gain).

tween the ages of about 9 and 14, potassium concentration continues to drop rapidly; this suggests that relatively less muscle mass is added with increasing age and weight. Accelerated muscular growth occurs in the male at puberty, giving rise to a second maximum in potassium concentration at about age 16. The absolute rate of muscular development, however, is even more pronounced than is indicated by the potassium values (since this is also a period of continuing rapid skeletal growth which would tend to lower the potassium concentration). The pronounced decline in potassium concentration in males between the ages of 16 and 20 was rather surprising, since this is a period during which the rate of weight gain is decreasing also. Evidently gain in weight after age 16 is a result of a "filling out" process involving the addition of fat, connective tissue, and bone, with relatively little addition of muscle tissue. The foregoing interpretation of changes in potassium concentration in males and females with age is quite in accord with observations of age and sex variations in total body water reported by Edelman *et al.* (8).

The steady decrease in potassium concentration beyond age 20, with similar

slopes for males and females (Fig. 1), is very interesting and worthy of further study. Multiplication of the potassium concentration by the average weight for each adult age group gives a measure of the amount of lean, oxidizing, protoplasmic mass and an indication of its variation with age and sex. Mean weights for the adult male age groups measured in our study showed essentially no increase in weight with age; therefore, the observed decrease in potassium concentration must represent a net loss in lean, protoplasmic mass. Between ages 20 and 60, this net loss in males amounted to about 18 percent. After correction for increase in gross body weight with increasing age, the net decrease in lean protoplasmic mass in females between ages 20 and 60 was only about 6 percent. This interpretation is in general agreement with observations of decrease in basal metabolic rate with increasing age (9) and supports von Döbelin's suggestion (10) that standard metabolic rate be expressed in relation to fat-free body mass.

Measurement of potassium-40 may offer an effective, statistical means of studying some aspects of the physiology of aging, exercise, starvation, and such wasting diseases as muscular dystrophy. The ease with which the potassium-40 measurements can be made [over 4000 people were measured, to a precision of 10 percent, during the recent 15-day Geneva Conference on Peaceful Uses of Atomic Energy, with an improved 2π counter (11) and counting time of 40 seconds] enhances the attractiveness of this method for the study of large population groups (12).

E. C. ANDERSON
W. H. LANGHAM

Los Alamos Scientific Laboratory,
University of California,
Los Alamos, New Mexico

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12. We are grateful to Mrs. B. E. Clinton for making the measurements on which this report is based. The cooperation of the many volunteer subjects is acknowledged, especially that of the Cub Scouts and Brownies who supplied data in the interesting region from ages 8 to 10. H. I. Israel was most helpful in programming for electronic data processing. This work was performed under the auspices of the U.S. Atomic Energy Commission.

30 April 1959

Changes in the Pattern of Nitrogen Excretion during the Life Cycle of the Newt

Abstract. In the course of its life cycle the eastern newt, *Triturus (Diemyctylus) viridescens*, undergoes two metamorphoses, the first from the aquatic larva to the terrestrial red eft; the second, 2 to 3 years later, from the eft to the permanently aquatic and sexually mature adult newt. The pattern of nitrogen excretion changes during both transformations. Older larvae excrete about 75 percent of the nitrogen as ammonia, 25 percent as urea; during the first metamorphosis the ratio of ammonia to urea is about 57:43; completely transformed efts excrete 87 percent of the nitrogen as urea. Adult aquatic newts show a partial return to the larval pattern, with an increase in the proportion of ammonia from the 13 percent typical for the eft to 26 percent, a highly significant difference.

The studies reported in this paper were inspired by G. Wald's article "The significance of vertebrate metamorphosis," which appeared in the 12 Dec. 1958 issue of *Science* (1). Wald emphasized the basic biochemical changes that occur during metamorphosis from aquatic to terrestrial existence, and that are correlated with morphological and ecological changes. He also stressed the occurrence of a "second metamorphosis" at the time of reproduction, and the return of many sexually mature vertebrates to their natal environment, which they had left during the first metamorphosis.

No other species of amphibia exhibits these two metamorphoses as strikingly as the eastern newt, *Triturus (Diemyctylus) viridescens*. During the first transformation, the aquatic larva changes into the terrestrial red eft, which, during its 2 or 3 years of life on land, shows many morphological adjustments to the new environment. The epidermis is roughened and covered by a thicker cuticle; numerous multicellular glands appear in the skin; the lateral-line organs sink below the surface and become nonfunctional; nasal glands of various types are formed; eyelids and lacrymal glands protect the eye against drying; the tongue becomes muscular, protrusible, and well equipped with glands whose secretion aids in the capture of prey.

At the end of its terrestrial growth

phase the eft has reached sexual maturity and migrates back to a pond, impelled by an increased output of one of the pituitary hormones, probably the lactogenic factor (2). In the laboratory, the metamorphosed animal (eft) can be sent back to the water at any time, beginning with the day when it first leaves the water, by implantation of one-half or one-quarter of an anterior lobe of an adult pituitary, or by injection of minimal amounts of a prolactin preparation. In contrast to other amphibians, which leave the water at the end of the breeding season, the adult newt remains in its pond permanently.

The morphological manifestations of the second metamorphosis are also numerous: the epidermis becomes smooth and covered with a thin cuticle; the lateral-line organs move to the surface and become functional once more; the tail acquires a broad keel; the tongue is reduced in size and no longer protrusible; the lingual glands are less prominent.

At the biochemical level, Wald found that the photosensitive pigment of the

eye, which in the eft is predominantly rhodopsin, as in other terrestrial vertebrates, is replaced by porphyropsin, which presumably was the pigment of the larval retina, as he demonstrated in tadpoles of the bullfrog *Rana catesbiana*.

A second, and functionally even more important, biochemical change takes place in all amphibia during the first metamorphosis from aquatic to terrestrial or amphibious life: a shift in the form in which nitrogen is excreted. Like other aquatic vertebrates, amphibian larvae excrete primarily ammonia. A terrestrial vertebrate must conserve water and cannot afford to use large amounts to eliminate the highly toxic ammonia. Nitrogen must be excreted in a more harmless form, which demands less water for its removal. Adult amphibia, like mammals, transform the ammonia into urea by the ornithine cycle, the essential step of which is the splitting of the arginine molecule into urea and ornithine by the enzyme arginase (3). The detailed studies of Brown and Cohen (4) on *Rana catesbiana* showed

that the change to ureotelism occurs simultaneously with a rise in activity of several enzymes of the ornithine cycle.

Munro (5) demonstrated that a similar change from ammoniotelism to ureotelism at metamorphosis occurs in the toad (*Bufo bufo*) and in two species of European newts (*Triturus vulgaris* and *T. cristatus*) and also in the Mexican axolotl when metamorphosis is induced in the latter by injection of thyroxine.

The close relationship between the biochemical metamorphosis and the change in habitat is strikingly shown by the excretory events that take place in the South African clawed frog, *Xenopus laevis* (5, 6). In the metamorphosing animal the excretory pattern changes: instead of excreting approximately 80 percent ammonia and 20 percent urea (typical for the tadpole), the animal excretes 50 percent ammonia and 50 percent urea. However, the young frog never leaves the water, and its nitrogen excretion returns to the earlier pattern (74 percent ammonia and 26 percent urea).

The existence of two clear-cut metamorphoses in *Triturus viridescens*, the first leading from water to land, the second back to water, suggested that a study be made of the pattern of nitrogen excretion in all three phases of its life cycle (7).

Larvae at various stages of development were starved for from 1 to 3 days and transferred in small groups to a tightly stoppered collection flask containing 6 ml of tap water, where they were kept for 48 hours. Samples of the water were then analyzed for ammonia and urea. Urine from red efts was obtained directly by gentle pressure applied to the region of the bladder. Adult newts were starved for 3 days, placed in separate flasks containing 7 ml of tap water each, and left for 10 hours. The percentage of total nitrogen (ammonia plus urea) excreted as ammonia and urea was determined by the Conway microdiffusion method, which had been used by Munro (5) and by Underhay and Baldwin (6).

The results are summarized in Fig. 1. The transition from a predominantly ammoniotelic excretion to a predominantly ureotelic pattern is gradual and is not completed until several weeks after metamorphosis. Most important, the adult aquatic newt shows a partial return to the larval pattern; the percentage of nitrogen excreted as ammonia rises from 13 percent in the eft to 26 percent in the adult. This difference is statistically highly significant and would be expected to occur by chance in less than 1 case in 10,000.

Thus, the biochemical events that occur during the second metamorphosis of the newt, when it returns from a ter-

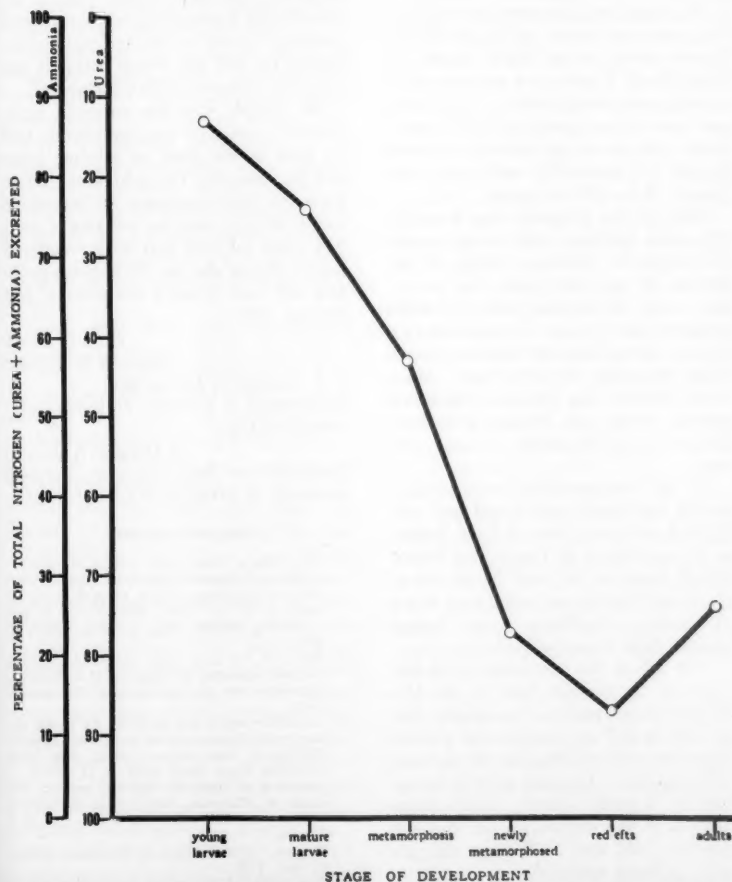


Fig. 1. Percentage of total nitrogen (urea plus ammonia) excreted as ammonia and urea in various stages of the life cycle of the newt.

restrial to an aquatic life, include not only the return to the larval form of retinal pigment but also a change in the mode of nitrogen excretion, in the direction of the larval pattern.

In *Triturus viridescens*, both metamorphoses can be modified experimentally with great ease. The first metamorphosis can be accelerated with thyroxine or suppressed by thyroidectomy in the embryo or by raising the larvae in solutions of thiouracil. The second metamorphosis can be precipitated, and practically fused with the first, by treatment with pituitary or prolactin. The patterns of nitrogen excretion under these experimental conditions will be investigated.

GERALD NASH
G. FANKHAUSER

Department of Biology, Princeton
University, Princeton, New Jersey

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7. This work was supported in part by a grant to Princeton University from the Gustavus and Louise Pfeiffer Foundation.

6 May 1959

Mummified Seal Carcasses in the McMurdo Sound Region, Antarctica

Abstract. Information was collected on 90 mummified carcasses of the "crabeater" seal in the ice-free areas of the McMurdo Sound region, Antarctica. The carcasses range from relatively well-preserved bodies to merely old, twisted, wind-dissected fragments of tissue. They are hard and dry and lie on the surface of the ground, mostly in valley bottoms. The arid, cold climate is ideal for retarding organic decay. One carcass was dated by radiocarbon analysis and found to be between 1600 and 2600 years old.

Mummified carcasses of the "crabeater" seal (*Lobodon carcinophagus*) lie scattered over the land surface 1 to 30 miles from the sea and up to 3000 feet above sea level in the ice-free areas of the McMurdo Sound region, Antarctica. A few such carcasses were noted on land many miles from the sea in this area almost 60 years ago by scientists of the early British antarctic expeditions (1). We noted 90 mummified seal carcasses during the 1957-58 field season (2). No doubt many others exist in the McMurdo

Sound region, and probably in other parts of Antarctica. The occurrence of these carcasses on the surface of the ground so far from their natural habitat raises the questions of why they are there, how long they have been there, and how they got there. Two carcasses have been shipped to the United States for anatomical and histological study. This paper represents a preliminary report of our observations (3).

All except one of the identifiable carcasses are of the crabeater seal. One is a Leopard seal (*Hydrurga leptonyx*) (4). A fairly well-preserved carcass of an Adelie penguin was found lying on the ground 15 miles from the sea near seal carcasses on the west side of the sound.

The leathery dry carcasses are in various states of preservation; some are relatively well-preserved, and others are merely old, twisted, wind-dissected fragments of tissue. The well-preserved ones range in length from 3½ to 7 feet and in diameter from 1 to 1½ feet. They are dry and hard, and they have hair only on the side in contact with the ground; this side is generally flat and has a strong smell.

We found seal carcasses in every ice-free area we visited in the McMurdo Sound region except Black Island and Ross Island. Twenty-five percent of the remains were found within a mile of the sea, but scattered groups of 2 to 19 specimens were found as much as 17 miles inland. The carcasses in each group were spaced 10 to 100 feet apart.

Most of the carcasses were found in the valley bottoms, many along courses of ephemeral streams. Most of the streams do not drain into the sea but into small, ice-covered lakes in valleys blocked from the sea by a moraine or a glacier. Several seal carcasses were found along the edges of these lakes. Many were found at the heads of ephemeral streams where the streams issue from glaciers, or at the heads of stream valleys.

All the carcasses noted were on land except one which was found half embedded in the ice cover of Lake Bonney at the upper end of Taylor Dry Valley. All of those on the land lie on top of the ground and most have 2 to 4 inches of coarse, windblown sand banked against their windward sides.

The age of the mummified seal carcasses in the ice-free land of the McMurdo Sound region is intriguing. The remains have been thought to be perhaps 100 years or so old, because the arid and cold climate of the area is ideal for retarding organic decay. Radiocarbon analysis of one carcass showed that it is between 1600 and 2600 years old; another is being analyzed.

The material, which was dated at the Lamont Geological Observatory, Colum-

bia University (sample L-462B), was from a brown, weathered fragment 1 foot wide and 4 feet long. It was found at an elevation of 1640 feet above sea level on glacial drift overlying a bedrock bench on the north side of Mount Nussbaum in Taylor Dry Valley. E. A. Olson and W. S. Broecker of Lamont Geological Observatory report as follows (5):

"Since the radiocarbon age of any organic sample requires a knowledge of initial radiocarbon concentration, it is customary to assume this to be the same as in a similar contemporary sample. In the case of antarctic seals, no present-day material was available, so that we have had to assume two extreme values and thus to quote an age interval rather than a discrete age. A lower age limit involves the assumption that the seal's diet consisted entirely of marine organisms deriving their carbon from surface water adjacent to Antarctica. Based on measurements of the dissolved carbonate in antarctic water which show it to be relatively depleted in radiocarbon, an age of 1700 (± 100) years is obtained. An upper limit of 2500 (± 100) years is obtained if the Lamont contemporary wood standard is used in the age calculation. Hence, the seal age almost certainly lies within the interval 1600-2600 years."

We believe that the antarctic seals, which occasionally wander inland, find no food in the fresh or alkaline lakes and therefore die. The cold, arid climate preserves their carcasses an incredible length of time, and the remains of seals and other animals that have wandered inland during the last 2000 years probably still exist to attest the animals' last journey (6).

TROY L. PÉWÉ
NORMAN R. RIVARD

U.S. Geological Survey and
Department of Geology, University of
Alaska, College

GEORGE A. LLANO
Committee on Polar Research, National
Academy of Sciences, Washington, D.C.

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4. Identified by David H. Johnson, curator, Division of Mammals, Smithsonian Institution, Washington, D.C., from a lower jaw of a carcass.
5. Written communication to the senior author, 16 Apr. 1959.
6. Publication of this article was authorized by the director of the U.S. Geological Survey.

15 July 1959

Ocean Water as a Source of Ice Nuclei

Abstract. Preliminary tests indicate that ocean water may release an abundance of ice nuclei to the atmosphere. These results may explain the observation that marked anomalies often accompany an influx of marine air in the Washington, D.C., area and the fact that abnormal counts are often associated with widespread precipitation.

The origin and nature of ultramicroscopic particles in the atmosphere which contribute to the formation of crystals (glaciation) in supercooled clouds and the effect of these nuclei with respect to subsequent rainfall remain obscure. Large fluctuations in the concentration of ice nuclei have been attributed to factors such as windblown dust and industrial effluents. Laboratory investigations summarized by Mason (1) have led to the tentative conclusion that ice nuclei active in natural clouds may be relatively insoluble substances of a rather special crystal structure, such as particles found in clay and other siliceous dusts. The evidence does not appear to be entirely consistent in this regard, particularly in the temperature ranges within which natural-cloud glaciation typically occurs. An extraterrestrial source for these nuclei was suggested by Bowen (2), who advanced the hypothesis that world-wide precipitation is enhanced about 30 days after meteor showers as a result of an increase in meteoritic debris which provides additional nuclei for the formation of ice crystals in accordance with the Bergerson-Findeisen ice-crystal growth mechanism.

Kline and Brier (3) summarized the few available series of daily observations on ice nuclei during several Januaries and indeed found a trend toward higher values around the dates on which such values are predicted by the meteoritic dust theory. However, pronounced increases in concentrations of ice nuclei, which were not associable with any known meteor showers, were detected on several days in February and March 1958 near Washington, D.C. We noted a tendency for higher counts to exist when the air at the surface came from easterly quadrants in the preceding 24 hours, a recent marine trajectory thus being implied. However, low concentrations also were observed during such flow regimes. Further observations during the past year suggest a relationship between the occurrence of high nuclei counts of ice nuclei and the total amount of precipitation over the United States in a 24-hour period. Widespread precipitation is of course frequently associated with moist air which has recently been in ocean areas.

Since it is known from the work of Junge (4) and others that the aerosol content of the atmosphere can be increased by a factor of at least 10 to 100 over marine storm areas, the question arises as to what role the state of the sea may play in the observed variations in concentration of ice nuclei. Birstein and Anderson (5) reported that sea salt might act as an ice nucleus at a threshold temperature of about -15°C . The aerosol was generated directly from sea salt in the crystalline state by grinding and heating procedures. But a short series of summer observations on the west coast of Ireland by Georgii and Metnieks (6) showed no obvious relationship between sea salt and ice nuclei. No further tests of the ice-nucleating properties of particles of marine origin are known to have been made, although hygroscopic particles from oceanic sources are known to be active nuclei for the condensation of water vapor to the droplet state.

Because of these uncertainties, we decided to perform experiments in which we would utilize a particle-generating mechanism analogous to the foaming and bubbling process associated with whitecaps. Bubbling action is known to produce salt particles, from the experiments reported by Mason (7) and others. About $\frac{1}{2}$ lit. of ocean water was placed in a bowl and agitated by the blades of an ordinary electric mixer. The air intake of a 10-lit. refrigerated expansion-type cloud chamber of the basic design described by Warner (8) was located a few inches above the foam and bubbles formed by the churning action of the blades. Figure 1 shows typical results compared with background counts obtained in an air mass that had recently been in a maritime tropical area. The fact that the warmest temperature observed for the commencement of nucleating activity with sea salt is comparable to that found in marine air in our local series of daily observations on ice nuclei may be significant. The use of carefully distilled water in lieu of ocean water gave negative results. Tests now under way tend to show that a number of soluble substances, including NaCl and MgCl_2 , yield counts of ice nuclei through this technique that are significantly higher than counts for the surrounding air.

Although these results do not shed much light on the meteor dust hypothesis and the observed recurrence of certain weather events on or near the same calendar date (weather singularities), they suggest a mechanism that might account in part for the high nuclei counts during periods of widespread precipitation, since such precipitation is frequently associated with general storminess and high surface winds. Wahl

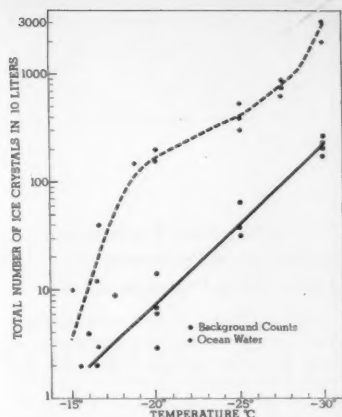


Fig. 1. Temperature-spectrum comparison between the number of ice nuclei in air samples drawn from near the surface of agitated ocean water and the number observed concurrently in ambient air. These data were obtained on 15 March 1959, during an influx of maritime tropical air in the Washington, D.C., area.

(9) has pointed out that the weather singularities in the month of January are closely related to changes in the general circulation, and Brier (10) indicated that during this month worldwide precipitation was at a maximum, during periods when there was the greatest transport of air at 50° north latitude at the earth's surface.

Although it is too early to generalize, these clues suggest that nucleation of natural clouds may be brought about in part by hygroscopic aerosols acting in the dual role of efficient condensation nuclei and ice nuclei. There is also a possibility that siliceous or other active nucleants may exist in colloidal suspension in certain oceanic areas due to erosion of the shore line by the action of wind, wave, and ocean currents, and that these nucleants are released to the atmosphere as minute particles. More direct identification techniques will be required to resolve the current uncertainties (11).

GLENN W. BRIER
DWIGHT B. KLINE

Office of Meteorological Research,
United States Weather Bureau,
Washington, D.C.

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- 13 May 1959

Effect of Strontium Replacement for Calcium on Production of Motile Cells in *Protosiphon*

Abstract. *Protosiphon botryoides* Klebs grows without evident zoosporegenesis in inorganic media in which strontium is substituted for calcium. Growth is 50 to 90 percent of that obtained with calcium; when sodium is substituted for calcium, there is no appreciable growth. Motility was observed at or above $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ levels of 5 mg/lit., with or without strontium.

Earlier reports of partial or complete substitution of strontium for calcium as a required nutrient in certain plant species (1) led, in connection with a study of the mineral nutrient requirements of *Protosiphon botryoides* Klebs, to an attempt to substitute $\text{SrCl}_2 \cdot 6\text{H}_2\text{O}$ in the growth medium for the $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ ordinarily supplied in Bold's inorganic salt medium for the culture of algae (2). Three treatments were set up, one with calcium chloride, a second with a molar equivalent of reagent-grade strontium chloride, and a third lacking both added calcium and strontium. A uniform inoculum, obtained from medium containing calcium was washed and added in equal

small quantities to each of the three preparations. The preparations were placed under illumination of approximately 300 ft-ca from cool white fluorescent bulbs at 22°C , under a light-dark cycle of 12 hours of light and 12 hours of darkness (3). By 12 days after inoculation a phototactic ring of *Protosiphon* cells, indicating zoospore formation, became evident in the preparation containing calcium chloride but did not appear in either of the other two preparations, although growth was evident in the medium containing strontium chloride. Microscopic examination of the cultures revealed an abundance of zoospores in the calcium-containing medium; however none were seen in the medium containing strontium. Turbidimetric growth measurements, reported as total cell volume per liter, were made 37 days after inoculation, with results shown as replicate 1 of Table 1. Subsequent replicates, which showed the same responses in relation to zoospore production, are also shown in the table.

That the growth of *Protosiphon* in the presence of the strontium chloride was not due directly to the addition of calcium as a contaminant in the strontium salt is clear from a study of the growth response to different levels of calcium chloride (Fig. 1) and from spectroscopic analysis of the reagent-grade strontium chloride used (4). The rate of growth in the strontium chloride was equivalent to what was obtained at a calcium level of about 0.4M equivalent, whereas the spectroscopic analysis revealed a calcium contamination of the reagent-grade strontium chloride of only 10 to

Table 1. Cell volume of *Protosiphon* in nutrient medium at end of culture period (ml./lit.).

Replicate	Medium		
	With Ca	With Sr	Without Ca or Sr
1	5.8	2.9	0
2	12.9	9.4	0
3	8.0	4.0	0
4*	7.7	6.9	0.7
5*	10.6	6.6	0

* Replicates with Specpure strontium salt.

20 parts per million. Replicates with Johnson Matthey, and Co.'s Specpure strontium salt containing 2 parts of calcium per million gave similar results. It appears that strontium replaces the major part, if not all, of the calcium required in this medium for optimum growth of *Protosiphon*, since the controls, containing all the other salts of the medium but the calcium or strontium salts, failed to sustain appreciable growth.

The two curves of Fig. 1 show the relative growth rate of *Protosiphon* at varying levels of calcium chloride. To maintain the chloride content uniform in these cultures, the calcium chloride was replaced by sodium chloride in one instance and by strontium chloride in the other. Other tests have indicated that results would have been similar if the sodium chloride replacement had been omitted from the medium. Careful microscopic examination of the cultures revealed that zoospore production, whether or not strontium was present, began at a calcium level of approximately 5 mg/lit., 0.2 the concentration of the calcium supplied in the basal medium.

The results of these studies on *Protosiphon* point to a critical role for calcium, which cannot be assumed by strontium, in the production of motile cells.

JOSEPH C. O'KELLEY
WALTER R. HERNDON

Biology Department,
University of Alabama, University

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28 April 1959

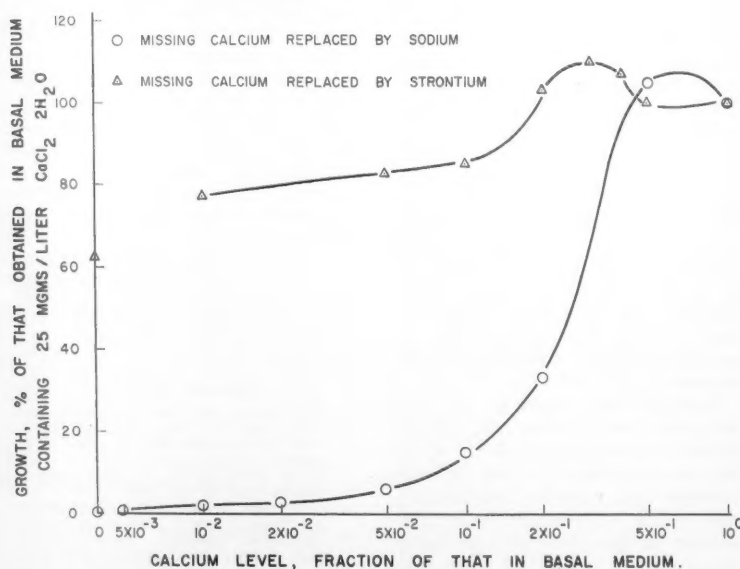


Fig. 1. Effect of strontium and sodium replacement of calcium on the growth of *Protosiphon botryoides* Klebs, measured as percentage of total cell volume obtained with 25 mg of $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ per liter.

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Estimates of Radiation Dose from Strontium-90 Due to Fallout

A recent article by Merrill Eisenbud, "Deposition of strontium-90 through October 1958," concludes, from consideration of the radiation delivered to bone marrow by the Sr^{90} absorbed by the bone from fallout debris, that "the maximum foreseeable dose [of radiation] from strontium-90 in the New York area is thereby estimated to be about 5 percent of the dose due to natural radioactivity" (1).

This conclusion appears to be inaccurate. In what follows it is shown that, instead, on proper calculation, Eisenbud's data lead to the conclusion that Sr^{90} -induced radiation to the bone marrow is, on the average, 15 to 60 percent of the natural background radiation. Some localized areas of bone marrow will receive considerably more intense radiation. Such calculations show also that the bone itself will receive, from Sr^{90} , radiation amounting to from 10 to 400 percent of the background radiation.

Eisenbud estimates that when Sr^{90} deposition due to fallout from past tests is at a maximum (in 1965), milk in the New York area will reach the level of $11 \mu\text{c}$ of Sr^{90} per gram of calcium, and that a child using this milk as a source of dietary calcium will develop a skeleton containing about $5.5 \mu\text{c}$ of Sr^{90} per gram of calcium (5.5 strontium units). For the purpose of this discussion this estimate is accepted as a first approximation, although, as shown below, it is probably too low. Eisenbud calculates, from the skeletal Sr^{90} level given above, the resultant radiation dose to the bone marrow. This dose is then compared with a value representing the dose from natural radiation, and it is concluded that the fallout radiation amounts to 5 percent of background radiation. Eisenbud's considerations of this matter are contained in the following paragraph from his article: "The United Nations Scientific Committee on the Effects of Atomic Radiation calculated . . . [(2)] that 1 micromicrocurie of strontium-90 per gram of calcium is equivalent to a dose of 1 millirem per year to the bone marrow. An individual having 5.5 micromicrocuries of strontium-90 per gram of calcium in his skeleton will therefore receive a dose of 5.5 millirems per year in addition to the dose from natural radiation of cosmic and terrestrial origin. According to the United Nations Scientific Committee, skeletal irradiation from natural sources is 125 millirems per year. The 5.5 micromicrocuries of strontium-90 per gram of calcium will therefore increase the natural dose to

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the bone marrow by about 5 percent."

According to the United Nations report (2, p. 9, Table 1, and p. 58, Table 25), the natural radiation to the *bones* is 125 to 130 mrem/yr, while the natural radiation to the *bone marrow* is 95 mrem/yr. Eisenbud's comparison appears to be between an estimated Sr^{90} radiation to the bone marrow and the natural radiation to the bone.

More properly, Sr^{90} and natural radiation ought to be compared relative to the same tissue, either bone or bone marrow. Such comparisons lead to the following results.

1) With regard to bone, according to the U.N. report (2, p. 107, par. 63), 1 μC of Sr^{90} per gram of calcium delivers to bone tissue 2.5 mrem/yr. Thus, 5.5 μC of Sr^{90} per gram of calcium will result in a bone dose of 13.8 mrem/yr, or about 10 percent of the natural dose (125 to 130 mrem/yr). This estimate refers only to an average value and assumes that the Sr^{90} is evenly spread throughout the skeleton. However, it has been shown by Engström *et al.* (3) that microscopic regions of the bone may receive a radiation dose about 40 times the average. Hence, these parts of the skeleton will receive from Sr^{90} a radiation dose amounting to about 400 percent of the radiation from natural sources.

2) With regard to bone marrow, a similar situation exists. This problem is considered in paragraphs 64 and 65 on pages 107 and 108 of the U.N. report (2). Paragraph 64 states: "In the following it will be assumed that 1 strontium unit [1 μC of Sr^{90} per gram of Ca] will cause a mean bone marrow dose rate of 1 mrem/yr. The true value of the mean marrow dose might however, be as low as 0.5 or as high as 2 mrem/year per strontium unit." The problem is further developed in paragraph 65, which states: "It should be emphasized that bone marrow cells which are almost surrounded by bone will receive doses which may be equal to those in compact bone. Taking into account all causes for non-uniformity, i.e. the non-uniform deposition in the mineralized zones, the variation in bone layer widths and geometrical factors [corners], the bone marrow level is probably five times the figures quoted above."

Eisenbud has chosen to employ, as the parameter relating Sr^{90} concentration to radiation dose, the ratio 1 mrem/yr per strontium unit. However this choice ignores the variability range (0.5 to 2 mrem/yr per strontium unit) given in paragraph 64 of the U.N. report, and the fivefold inhomogeneity factor cited in paragraph 65. If all the relevant data in the U.N. report are considered, we reach the conclusion that an average skeletal burden of 5.5 μC of Sr^{90} per

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gram of calcium will deliver to localized regions of the bone marrow between 14 (5.5 strontium units \times 0.5 mrem/yr per strontium unit \times 5) and 55 (5.5 strontium units \times 2 mrem/yr per strontium unit \times 5) mrem/yr. When these dose rates are compared with the natural rate of 95 mrem/yr, we find that Sr^{90} will contribute to the bone marrow additional radiation amounting to about 15 to 60 percent of the radiation from natural sources.

The foregoing considerations are based only on the sources of data employed by Eisenbud. If other pertinent informa-

tion is taken into account the above conclusion becomes modified further. As pointed out with reference to a recent estimate of the expected dietary Sr⁹⁰ levels in St. Louis (4), data reported by H. P. Straub of the U.S. Public Health Service to the recent hearings on fallout before the Joint Committee on Atomic Energy show that about one-third of dietary Sr⁹⁰ comes from non-milk sources. Since these sources, principally cereals and vegetables, have Sr⁹⁰ concentrations considerably higher than those of milk, the total dietary Sr⁹⁰ level with which bone is in equilibrium is

higher than is indicated by estimates based on milk alone. Consideration of this factor would increase the foregoing estimates of Sr^{90} radiation to bone and bone marrow by a factor of about 50 percent. In addition, as Caster (5) has pointed out, calculations by Engström *et al.* (3) indicate that a heterogeneity factor of 40 to 60 (as against the value of 5 suggested in the U.N. report) may be operative in some conditions. In this case the effect of Sr^{90} relative to natural radiation would be increased proportionately.

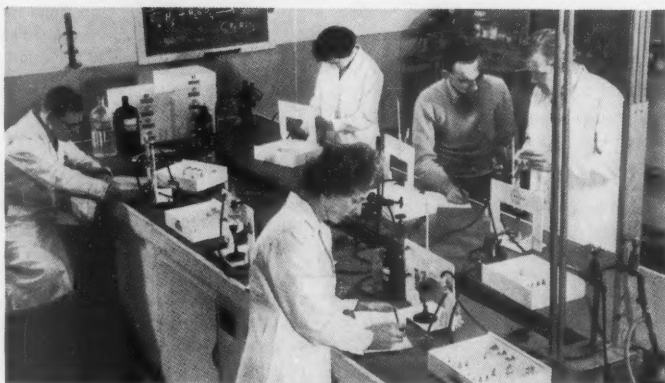
In sum, Eisenbud's conclusion appears significantly to underestimate the relative effect of radiation from Sr^{90} resulting from fallout due to nuclear explosions. Since Eisenbud's article is part of the testimony before the recent hearings on fallout before the Joint Committee on Atomic Energy, consideration should be given to appropriate means of correcting the record of these hearings.

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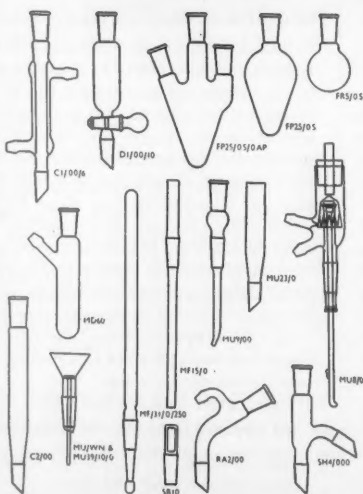
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Commoner's principal criticisms of my article are (i) that my dose estimates did not allow for inhomogeneities in Sr⁹⁰ deposition or for the ranges in the published estimates of dose per strontium unit, and (ii) that I underestimated the dose from Sr⁹⁰ by assuming that the isotope is derived by human beings from dairy sources only.

In addition to these two points, which I will discuss further, Commoner calls attention to my reference to 125 mrem/yr as the natural "skeletal" radiation dose. The dose to the *bone marrow* from natural sources was actually assumed to be 95 mrem, the value I used in concluding that 5.5 mrem/yr is "about 5 percent" of the dose from natural sources. The value of 125 mrem/yr to the *bone* was given redundantly in the text. I am indebted to Commoner for calling this to my attention.

The method I used in estimating the dose to bone marrow was adopted directly from the procedures developed by the United Nations Scientific Committee on the Effects of Atomic Radiation. It is significant that this committee relied on bone marrow dose rather than on osteocyte dose in calculating the biological consequences of Sr⁹⁰ deposition. It is true that, as Commoner says, the



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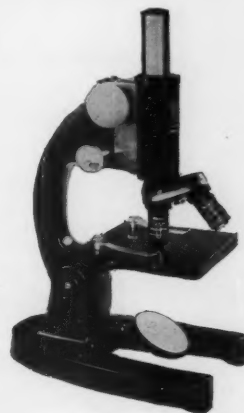
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use of 1 mrem/yr per strontium unit "ignores" the range of estimates given in the United Nations report (0.5 to 2 mrem/yr per strontium unit), but I considered the assumed value to be a satisfactory basis for tissue dose approximation, as indeed did the U.N. Radiation Committee in the calculations for their report. Commoner notes also the five-fold inhomogeneity to which the U.N. report refers, and he states that I should have used this in my computation. Again, the U.N. Committee simply pointed out that this inhomogeneity probably exists, but they did not find it necessary to include this factor in the computations either of dose or of the biological consequences of Sr⁹⁰ deposition.

The doses we are discussing are very much less than the smallest dose required to produce observable effects in the laboratory. Commoner's concern with the significance of these doses derives from the concept that prudence in estimating the possible consequences of the exposure of large populations to small doses of radiation requires one to assume that there is no threshold, and that the biological consequences of radiation doses, however small, can be estimated by a linear extrapolation of existing experimental data. This concept is not applied to all of the biological effects of radiation and is not accepted by many investigations of Sr⁹⁰ toxicity as being applicable to the carcinogenic effects of this isotope.

It is not my purpose to argue for or against this concept but merely to note that it exists and serves as the basis of the concern which Commoner and others have experienced over the possible consequences of small doses of Sr⁹⁰. This being so, I am puzzled that Commoner continues to emphasize the importance of inhomogeneities in deposition of Sr⁹⁰ at dose levels of the order of a few millirems per year. It is true that the portion of the bone marrow in which more than the average amount of the isotope is deposited receives more than average irradiation. The non-threshold, proportional theory would suggest that the probability of carcinogenesis would thus be increased correspondingly within that portion of the marrow. However, it is likewise true that the remaining portion of the tissue will have less than the average dose and, for this remaining portion, the probability of carcinogenesis will be lessened. According to the proportional theory, the probability of a carcinogenic response in a given volume of tissue should be a function of the total energy absorbed within the tissue.

Commoner's criticism of my use of milk as the basis for computing potential risk does have merit. Foods other than dairy products have been shown recently to be

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contributing increasingly large proportions of Sr^{90} to the diet, and this factor should be considered in future computations. Whether or not omission of this factor does in fact imply that I underestimated the dose by a factor of 0.5, as suggested by Commoner, I cannot say at this time.

It is my opinion that "about 5 percent" is a reasonable estimate of the maximum increase in bone marrow dose to be expected. "About 5 percent" could mean that the actual levels would be as much as 10 percent, but in my opinion, it is more likely that the true values will prove to be somewhat lower than 5 percent. This is because the method I used to compute future doses does not allow for the effect of foliar deposition or the possibility that Sr^{90} in soil will become less available to plants over a period of many years.

MERRIL EISENBUD

U.S. Atomic Energy Commission,
New York Operations Office, New York

Teaching and Research

The point that Jesse D. Rising raises [*Science* 130, 66 (10 July 1959)]—that "many potentially excellent teachers may be doing less than their best teaching in an effort to satisfy the university administration by doing research"—was answered forcefully by an experienced teacher in these words:

"In the life of a university department the interests of research and of teaching are competitors. . . . The activities themselves are in necessary conflict in any department which thus seeks to serve two masters. The activities compete for room space, for the working time of staff members, including mechanics and secretaries, for funds, and for the control of faculty appointments. . . .

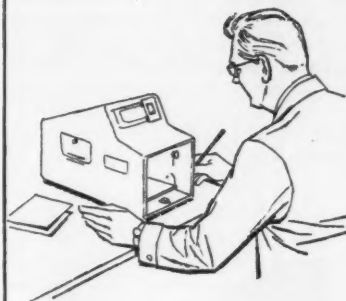
"In my experience the demands of teaching and of research have been in continual conflict for nearly forty years, and I cannot remember that either function ever helped the other. Many a demonstration would have been better prepared and many a student better served if the urgency of some situation in the research laboratory (and the fascination of it) had not pulled in that direction. On the other hand, the continuous concentration that a research dilemma can demand was often broken up by the class bell. I would have done better at either one of these activities if I had kept out of the other, and I suspect that there are hundreds of scientific men who could give the same testimony. This is not a situation that we can take any satisfaction in but is just one of the facts of academic life. . . .

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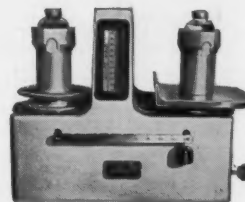
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swing the protective tariff back from the researchers to the teacher as teacher. . . ."

These quotations come from a speech by Paul Kirkpatrick of Stanford University, delivered at a meeting of the American Physical Society in New York last January. They state in better words than many of us can muster the opinion prevailing among many teachers of undergraduate college physics and are worthy of more publicity than they have been given.

URBAN E. SCHNAUS

Department of Physics,
Catholic University, Washington, D.C.

Liesegang Phenomenon

In a recent report [*Science* 129, 1365 (1959)], Van Oss and Hirsch-Ayalon claim that the Hirsch effect constitutes the proper explanation of the Liesegang phenomenon. This claim is based on the assumption that the Liesegang rings act as membranes which prevent further diffusion of the reacting substances. These authors also cite experimental evidence (see their references 9 and 21) in support of their conclusion that the rings remain impermeable to the diffusing outer (presumably more concentrated)

reactant until the other (inner) reactant is exhausted in the vicinity of the ring.

Although it is generally agreed that the medium is exhausted of this reactant in the vicinity of the ring, the evidence for the impermeability of the ring is by no means conclusive. The Liesegang phenomenon is equally well explained [see, for example, Wagner, *J. Colloid Sci.* 5, 85 (1950)] if a critical ion-product concentration, such as a supersaturation product, is required as a necessary condition for ring formation. In that case the clear spaces between the rings merely result from the lowering of the inner electrolyte concentration by adsorption on the last ring or by counterdiffusion. As a result, the outer electrolyte must then diffuse for some distance until the critical concentration is again reached.

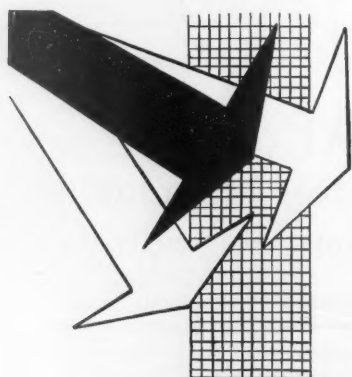
Another argument against accepting the Hirsch effect as the *only* explanation of Liesegang rings under all conditions is found in the experiments by Morse [*J. Phys. Chem.* 34, 1554 (1930)] in which rings of rather widely spaced crystals were formed in water without any colloidal material present. It seems a little farfetched to suppose that these rings act as membranes.

Van Oss and Hirsch also state that Ostwald's supersaturation theory is refuted by Hatchek's experiments. The arguments against this view have already been presented in some detail [K. H. Stern, *Chem. Revs.* 54, 79 (1953)]. Basically they amount to this: that supersaturation can exist in the presence of crystals, particularly if these are well dispersed; and that under these conditions rings still form because the rate of crystal growth is less than the diffusion velocity of the reactants. When the rings consist of very small crystals, closely spaced, the Hirsch effect may very well operate.

KURT H. STERN

Department of Chemistry,
University of Arkansas, Fayetteville

As the title of our report, "An explanation of the Liesegang phenomenon," implies, we did not claim to advance an explanation that excludes all other explanations. It is indeed quite probable that in certain cases diffusion, supersaturation, or even gel-protection effects play their role. Still, as we pointed out, Liesegang bands have been known to occur under circumstances where these effects were lacking. Now, although it remains difficult to ascertain which effect predominates in the formation of any particular set of Liesegang bands, the Hirsch effect can in a general way satisfactorily account for all the circumstances under which Liesegang bands are formed, needing no assumptions on diffusion, supersaturation, or gel protection. The Hirsch effect, an experimentally established and



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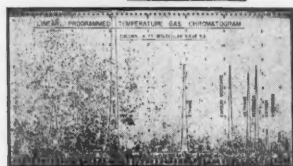
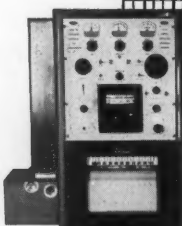
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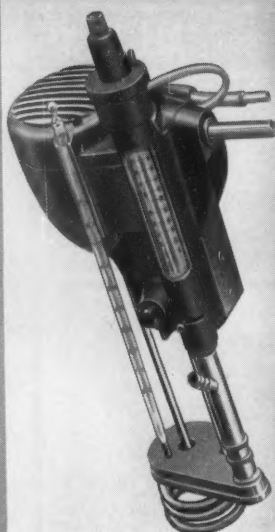
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general phenomenon, must give rise to Liesegang bands exactly under those circumstances where these bands actually occur.

The role of the gel or membrane in the Hirsch effect must not be overestimated, the effect itself being independent of the presence of colloid material. Only for the quantitative measurement of the Hirsch effect are carrier membranes, or other porous walls, used to advantage, principally to avoid convection.

The Hirsch precipitates are best considered as barriers to the forming ions rather than as membranes. Actually, by the time Liesegang layers appear and can be inspected, they have already lost their property as barriers (except for the last layer, if one is quick enough). Thus, the occurrence of bands of widely spaced crystals in water does not exclude a Hirsch effect.

C. J. VAN OSS

Laboratory of Physical Biochemistry,
National Veterinary College,
Alfort, France

Radioactive Fallout

Your issue of 22 May [*Science* 129, 1412 (22 May 1959)] contained an assessment, issued by the General Advisory Committee of the Atomic Energy Commission, of the dangers to the human race of radioactive fallout. Without discussing the obvious impertinence of a collection of physicists, chemists, engineers, and what-have-you who presume to issue a pronouncement on a crucial biological question, I should like to offer comment on certain of the points which they raised.

1) The fact that "the amount of total body external radiation resulting from fallout to date, together with future fallout . . . from previous weapons tests, is: (i) less than 5 percent as much as the average exposure to cosmic rays and other background radiation" is repeated ad nauseam to reassure the public. However, this argument is a red herring designed to deceive. The principal dangers (both physiological and genetic) to the human race from fallout stem from the decay of the radioactive fallout material after it has been taken into the body and incorporated within certain cells and tissues. That the total quantity of radiation reaching the whole body from outside is far greater is largely irrelevant to the question of the potential dangers of fallout from nuclear tests. Throwing rubber balls at a person is not an intelligent way of finding out what would happen were he to swallow one.

2) With respect to the internal effects of strontium-90, they comfort us with the statement that "the amount of strontium-90 which has been found in food and water is less of a hazard than the

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amount of radium normally present in public drinking water supply in certain places in the United States." Since it is impossible to assess as yet the effects in man of ingestion of Sr^{90} , which has been a factor in human ecology only since 1954, one wonders how they can be so sure that it is "less of a hazard" than radium or anything else. Doctors who were prescribing radium for a variety of conditions as recently as the 1920's were also sure that there was no hazard involved, but many people died of it nonetheless. We shall all await publication of the studies on the high-radium drinking water to which the committee refers, but until we have had the opportunity to study them we had better treat this statement with the same suspicion which we have learned to extend to all other reassuring pronouncements emanating from the Atomic Energy Commission and its creatures.

Meanwhile, I should like to offer the following comment on the hazard of Sr^{90} , in order to solicit a refutation by the committee; I suggest only that they consult a biologist first, and if they are not acquainted with any I should be delighted to suggest one or two.

Since 1955, the maximum permissible body burden for Sr^{90} has been set at 1 μC (I cannot find publishable words with which to comment on the fantastic action of the U.S. National Committee on Radiological Protection, which recently doubled this, to 2 μC). In their book, *Bone and Radiostrontium* (Wiley, New York, 1957), Engstrom *et al.* state that a total body concentration of 1 μC of Sr^{90} would be expected to deliver, in approximately 10 years, roughly 1000 r to certain microscopic hot spots located in the spongy bone, close to the marrow, where the blood-forming tissues are located. (One thousand roentgens was about the whole-body dose absorbed by the Austrian miners of Joachimsthal over a 17-year period, the mean time required for the development of the fatal lung cancers which used to kill three-quarters of them). In view of this calculation, Engstrom *et al.* recommended that the maximum permissible body burden be reduced to 0.1 μC , a recommendation which, I understand from *Science* [129, 1473 (29 May 1959)], has been adopted by the International Commission on Radiological Protection.

If the maximum permissible body burden for workers known to be subjected to radiation hazards is 0.1 μC , that for the population at large should be reduced, according to the International Commission, by one order of magnitude—that is, to 0.01 μC .

In the recent article by Kulp *et al.* [*Science* 129, 1249 (8 May 1959)], we learn that children seem to have on the average about three times the concentration of Sr^{90} in their bones that adults

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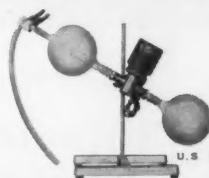
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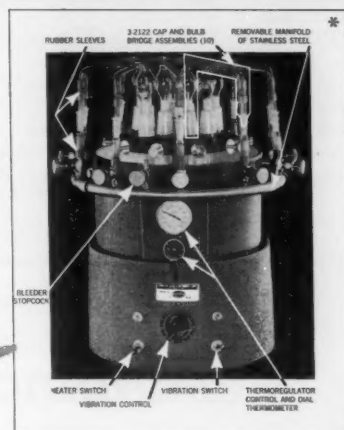
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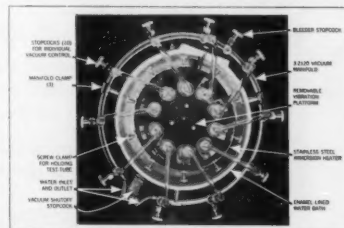


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have; 1-year-old infants have some eight to ten times the adult concentration. In view of this, and since the biological effects of radiation are more serious on rapidly growing and metabolizing cells, it seems to me that a separate maximum permissible body burden should be set for children, at approximately 0.003 μC .

That this figure is not unreasonably low is apparent in studying data from some Russian studies (cited by Engstrom *et al.*) on the effects of injecting small amounts of Sr^{90} into dogs; these animals developed bone cancers approximately 3 years after injection of 0.0001

μC of Sr^{90} per gram. Engstrom *et al.* calculate that the retained dose in a 10-kg dog would be of the order of 0.01 to 0.1 μC . Now, a 1-year-old child weighs approximately 10 kg, and it seems evident, to me at least, that its maximal skeletal concentration must not be permitted to reach the order of concentration of Sr^{90} known to cause fatal bone cancers in dogs.

We learn from the article by Kulp *et al.* that in 1966, when the highest skeletal concentration of Sr^{90} in young children will occur, some 1 percent of the world's children are expected to have a

skeletal concentration of 20 μC per gram of calcium. Since the average 1-year-old infant, weighing 10.6 kg, has roughly 100 g of calcium in his body, it follows that in 1966 1 percent of these children will have a total Sr^{90} skeletal level of 0.002 μC , and beyond doubt a significant fraction of 1 percent (hundreds of thousands, millions?) will have exceeded our suggested limit of 0.003 μC , and some may have skeletal concentrations of the order of those known to cause cancer in dogs.

This happy picture is based on the optimistic assumption that no further testing of nuclear weapons will occur (and neglects to consider the effect of other radioactive fallout elements). But what if nuclear tests continue?

J. GORDIN KAPLAN

Department of Physiology, Dalhousie University, Halifax, Nova Scotia

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Imprinting

Eckhard Hess, in his stimulating survey of recent progress in studies of imprinting [*Science* **130**, 133 (1959)] referred briefly to his inability to attain auditory imprinting with mallard ducks, *Anas platyrhynchos*. He did not mention, however, that it has been possible to attain auditory imprinting with other species—for example, *Aix sponsa*, the wood duck [P. H. Klopfer, *Ecology*, **40**, 90 (1959)].

This point would not ordinarily be of great significance except that it illustrates the importance of attending to interspecific differences in the survival value of particular kinds of behavior. Hess' paper shows the wild mallard to be an excellent imprinter, while the wood duck is considered to be poor. But, if auditory rather than visual stimuli are used, quite the reverse situation obtains. To a zoologist this seems reasonable: mallards nest in comparatively open situations, wood ducks in holes recessed in trees. Mallard young can see their mother when she first leaves the nest, the wood duck young cannot. Thus, the seeming importance of visual patterns for imprinting may be a reflection of the dominant sensory modality of the subjects rather than a characteristic of a particular type of behavior. In fact, one of the earliest reports on this subject dealt with olfactory imprinting [W. H. Thorpe and F. G. W. Jones, *Proc. Roy. Soc. (London)* **B124**, 56 (1937)]. The importance of olfaction to most mammals should suggest that it would be a mistake to confine further work in this area to the otherwise ingenious apparatus devised by Hess.

PETER H. KLOPFER

Duke University,
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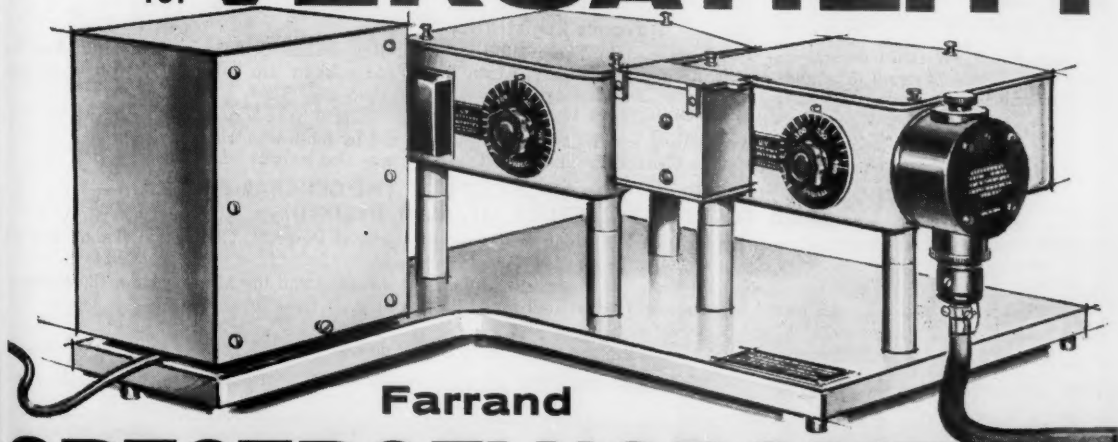
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- b) The General Program of the Annual Meeting, c. 200 pp., which will appear early in December.

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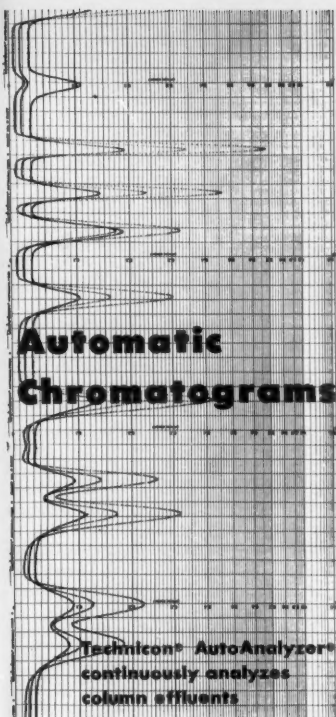
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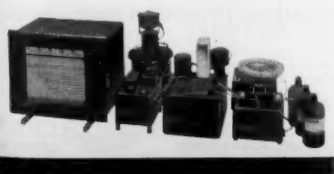
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Peter Klopfer's comments concerning my article are worth noting but do not precisely relate to my findings. Certainly we obtained auditory imprinting in the mallards, as well as in other species, since sound is used in our presentation along with the visual object. What we were not able to demonstrate for the mallard was *auditory imprinting in the egg*.

ECKHARD H. HESS
University of Chicago, Chicago, Illinois

Strontium-90 Levels and Wheat

In "Strontium-90 in man III" by Kulp, Schultert, and Hodges [*Science* 129, 1249 (1959)], "the widespread flow of wheat and powdered milk from the Northern to the Southern Hemisphere" is suggested as a possible explanation for the smaller difference in the strontium-90 levels in bone than in recorded fallout between the two hemispheres.

As related to wheat, at least, this is highly questionable. Argentina and Australia are two of the world's principal wheat exporters. A cursory review of the FAO *World Grain Trade Statistics* indicates that in 1956-57, the latest crop year for which full data are available, movement of wheat (including the wheat equivalent of flour) from the Northern to the Southern Hemisphere was on the order of 1220 thousand metric tons, as compared with a movement of 4300 thousand metric tons of Southern Hemisphere wheat into the Northern Hemisphere. Another 2500 thousand metric tons moved between Southern Hemisphere countries, the largest share of this local trade being represented by Argentine exports to Brazil (1040 thousand metric tons) and Australian exports to New Zealand (340 thousand metric tons). Indonesia, Singapore-Malaya, Ecuador, and the Belgian Congo as well as Brazil are here considered Southern Hemisphere countries, although part of each is in the Northern Hemisphere.

If strontium-90 is moving across the equator in wheat, it would appear probable that the net movement is northward rather than southward.

JAMES J. PARSONS
Department of Geography,
University of California, Berkeley

We appreciate the correction of Parsons showing that the net flow of wheat, if not of powdered milk, is from the Southern to the Northern Hemisphere. Flow in either direction is, of course, equally effective in bringing the strontium-90 content of human bone toward a mean, so that the North-South ratio of strontium-90 concentration in human

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bone is less than the North-South ratio of cumulative fallout.

The case of Australia is puzzling since the Australians subsist almost entirely on their own foodstuffs yet the average bone level in 1957-58 (0.20 μmc of Sr^{90} per gram of calcium) was equal to that in the United States. Other climatic and agricultural factors must play a more dominant role here if the bone sampling is representative (1).

J. LAURENCE KULP
ARTHUR R. SCHULERT
ELIZABETH J. HODGES

Lamont Geological Observatory,
Torrey Cliff, Palisades, New York

Note

1. This is Lamont contribution No. 372.

Church-Affiliated Colleges

Donald L. Thistlethwaite [*Science* 130, 71 (1959)] has reported that religious affiliation on the part of a college is negatively related to encouraging Ph.D. scholars in the natural sciences.

It has occurred to me that this factor may have an important bearing on his ranking of institutions by geographical region, especially since his sampling is so extensive and since some of these regions

have a much higher proportion of church-supported institutions than do others.

An illuminating extension of this study would be a subclassification of geographical ranking according to whether or not the institutions included in the sample have religious affiliation.

JAMES R. KUPPERS
Grifton, North Carolina

To test the hypothesis suggested by Kupperts I have done a two-way analysis of variance. In order to avoid cells with missing entries, it was necessary to combine the New England and Middle Atlantic regions. Thus we have a 2 by 4 classification: presence versus absence of religious affiliation and separation by four regions. The results indicate significant differences in the production of graduates who attain the Ph.D. in the natural sciences ($p < .01$) between geographical religious-affiliation groups, but no significant interaction. The nonsignificant interaction indicates that the geographical differences have not been found to vary according to whether or not the colleges have religious affiliations.

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Meetings

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14-17. American College of Chest Physicians, 25th, Albuquerque, N.M. (M. Kornfeld, 112 E. Chestnut St., Chicago 11, Ill.)

15-16. American Ceramic Soc., Glass Div., Wernersville, Pa. (F. P. Reid, ACS, 4055 N. High St., Columbus 14, Ohio.)

15-17. Academy of Psychosomatic Medicine, Cleveland, Ohio. (B. B. Moss, Suite 1035, 55 E. Washington St., Chicago 2, Ill.)

15-17. National Soc. of Professional Engineers, fall meeting, Seattle, Wash. (P. H. Robbins, NSPE, 309 Bancroft Bldg., Univ. of Nebraska, Lincoln.)

16-17. Association of Midwest College Biology Teachers, conf., Notre Dame, Ind. (G. R. Bernard, Dept. of Biology, Univ. of Notre Dame, Notre Dame, Ind.)

17-18. American Acad. of Psychotherapists, 4th annual conf., New York, N.Y. (AAP, 30 Fifth Ave., New York 11.)

17-25. Plastics Industry, intern. fair, Düsseldorf, Germany. (Nordwestdeutsche Ausstellungs Gesellschaft (NOWEA), Ehrenhof 4, Düsseldorf.)

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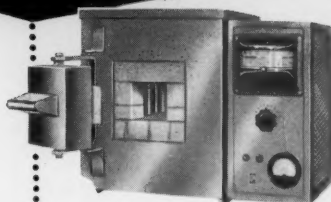
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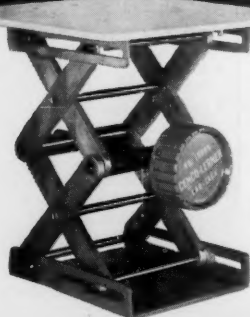


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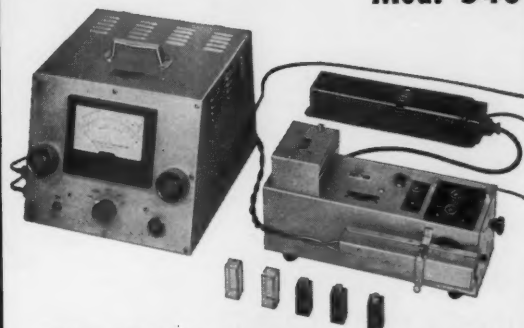
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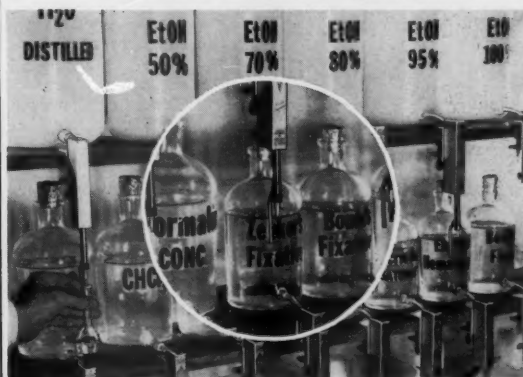
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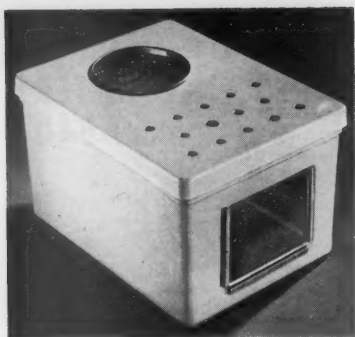
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18-23. American Soc. of Plastic and Reconstructive Surgery, Miami Beach, Fla. (T. R. Broadbent, 508 E. South Temple, Salt Lake City, Utah.)

19-21. High Polymer, 9th Canadian, Toronto, Ontario, Canada. (K. E. Russell, Dept. of Chemistry, Queen's Univ., Kingston, Ontario.)

19-22. Semiconductor Symp. (Electrochemical Soc.), Columbus, Ohio. (A. C. Beer, Battelle Memorial Inst., 505 King Ave., Columbus 1, Ohio.)

19-23. American Public Health Assoc., 87th annual, Atlantic City, N.J. (B. F. Mattison, 1790 Broadway, New York 19.)

19-23. American Soc. of Civil Engineers, annual conv., Washington, D.C. (W. H. Wisley, ASCE, 33 W. 39 St., New York 18.)

19-23. Radioisotopes in the Biosphere, symp., Minneapolis, Minn. (R. B. Caldecott, Center for Continuation Study, Univ. of Minnesota, Minneapolis 14.)

19-31. International Cong. of Therapeutics, Strasbourg, France. (Prof. Fontaine, Doyen de la Faculte de Starsbourg, France.)

19-31. Pan American Medical Assoc., 10th conf., Mexico, D.F., Mexico. (J. Eller, PAMCA, 745 Fifth Ave., New York 22.)

20-21. Reprocessing of Nuclear Fuels, AEC symp., Richland, Wash. (J. T. Christy, Hanford Operations Office, U.S. Atomic Energy Commission, Richland, Wash.)

20-22. Standards, 10th natl. conf., Detroit, Mich. (K. G. Ellsworth, American Standards Assoc., 70 E. 45 St., New York 17.)

20-23. Clean Air, intern. conf., London, England. (National Soc. for Clean Air, Palace Chambers, Bridge St. London, S.W.1, England.)

22-24. Acoustical Soc. of America, fall meeting, Cleveland, Ohio. (W. Waterfall, ASA, 335 E. 45 St., New York 17.)

22-24. American Documentation Inst., annual, Bethlehem, Pa. (C. G. LaHood, Jr., Library of Congress, Washington 25.)

22-25. British Medical Assoc., annual clinical, Norwich, England. (W. Hedcock, BMA House, Tavistock Sq., London, W.C.1, England.)

23-24. Canadian Soc. for the Study of Fertility, Montreal, Canada. (J. F. Campbell, 238 Queen's Ave., London, Ont., Canada.)

23-25. American College of Cardiology, 8th annual, Philadelphia, Pa. (P. Reichert, ACC, Empire State Bldg., New York 1.)

23-27. American Heart Assoc., annual, Philadelphia, Pa. (W. F. McGlone, AHA, 44 E. 23 St., New York 10.)

24-29. Darwin Centennial, intern. celebration, Chicago, Ill. (Office of Public Relations, Univ. of Chicago, Ill.)

24-29. First All-India Cong. of Zoology, Jabalpur. (B. S. Chauhan, Zoological Survey of India, 34 Chittaranjan Ave., Calcutta 12.)

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York, N.Y. (ACS, 521 W. 57 St., New York 19.)

26-27. Griseofulvin and Dermatomycoses, intern. symp., Miami, Fla. (H. Blank, Dept. of Dermatology, Univ. of Miami School of Medicine, Miami 36.)

26-28. Aeronautical and Navigation Electronics, IRE conf., Baltimore, Md. (L. G. Cumming, IRE, 1 E. 79 St., New York 21.)

26-28. Analytical Chemistry in Nuclear Reactor Technology, 3rd conf., Gatlinburg, Tenn. (C. D. Susano, Oak Ridge Natl. Lab., P.O. Box Y, Oak Ridge, Tenn.)

26-28. Gas Lubricated Bearings, 1st intern. symp., Washington, D.C. (S. W.

Doroff, Power Branch, Office of Naval Research, Washington 25.)

26-28. National Rehabilitation Assoc., Boston, Mass. (E. D. Callahan, 14 Court Square, Boston 8.)

26-28. Society of Automotive Engineers, natl. transportation meeting, Chicago, Ill. (R. W. Crory, SAE, 485 Lexington Ave., New York 17.)

26-30. Society of Photographic Scientists and Engineers, natl. conf., Chicago, Ill. (SPSE, Box 1609, Main Post Office, Washington, D.C.)

26-30. Standardization (ISO), committee on rubber, New York, N.Y. (ISO, General Secretariat, 1, rue de Varembe, Geneva, Switzerland.)

27. Association of Consulting Chemists and Chemical Engineers, annual symp., New York, N.Y. (A. B. Bowers, ACCCE, 50 E. 41 St., New York 17.)

28-29. Computer Conf., Chicago, Ill. (F. A. Judd, Armour Research Foundation, Technology Center, 10 W. 35 St., Chicago 16, Ill.)

28-30. Aircraft Electrical Soc., Los Angeles, Calif. (E. I. Niles, AES, 920 South Robertson Blvd., Los Angeles 35.)

28-31. American Soc. of Tropical Medicine and Hygiene, Indianapolis, Ind. (R. B. Hill, 3575 St. Gaudens Rd., Miami 33, Fla.)

29-31. Animal Care Panel, 10th annual, Washington, D.C. (Animal Care Panel (ILAR), NAS-NRC, 2101 Constitution Ave., NW, Washington 25.)

30-31. Society for the Scientific Study of Religion, New Haven, Conn. (J. E. Dittes, 409 Prospect St., New Haven 11, Conn.)

30-31. West Central States Biochemical Soc., Columbia, Mo. (D. F. Millikan, WCSBS, Dept. of Horticulture, College of Agriculture, Univ. of Missouri, Columbia.)

November

1-4. Society of Economic Geologists, Pittsburgh, Pa. (H. M. Bannerman, U.S. Geological Survey, Washington 25.)

2-4. Atomic Industrial Forum, annual conf., Washington, D.C. (Atomic Industrial Forum, Inc., 260 Madison Ave., New York 16.)

2-4. Geochemical Soc., Pittsburgh, Pa. (K. B. Krauskopf, Geology Dept., Stanford Univ., Stanford, Calif.)

2-4. Geological Soc. of America, Pittsburgh, Pa. (H. R. Aldrich, 419 W. 117 St., New York 27.)

2-4. Mineralogical Soc. of America, Pittsburgh, Pa. (C. S. Hurlbut, Jr., 12 Geological Museum, Harvard Univ., Oxford St., Cambridge 38, Mass.)

2-4. National Assoc. of Geology Teachers, Pittsburgh, Pa. (F. Foote, Dept. of Geology, Williams College, Williamstown, Mass.)

2-4. Paleontological Soc., Pittsburgh, Pa. (H. B. Whittington, Museum of Comparative Zoology, Harvard Univ., Cambridge 38, Mass.)

2-5. Physical and Extractive Metallurgy, symp., Chicago, Ill. (Metallurgical Soc. of AIME, 29 W. 39 St., New York 18.)

2-6. American Inst. of Mining, Metallurgical, and Petroleum Engineers and Inst. of Metals, fall, Chicago, Ill. (E. O. Kirkendall, AIME, 29 W. 39 St., New York 18.)

2-6. Collegium Internationale Allogogicum, 4th symp., Rome, Italy. (A. Cerletti, Pharmacological Laboratories, Sandoz Ltd., Basel, Switzerland.)

4-5. Diffraction, 17th annual conf., Pittsburgh, Pa. (P. K. Koh, Allegheny Ludlum Steel Corp., Research and Development Laboratories, Brackenridge, Pa.)

4-6. American Nuclear Soc., conf., Washington, D.C. (American Nuclear Soc., John Crerar Library, 86 E. Randolph St., Chicago 1, Ill.)

4-6. Antibiotics, 7th annual symp.,

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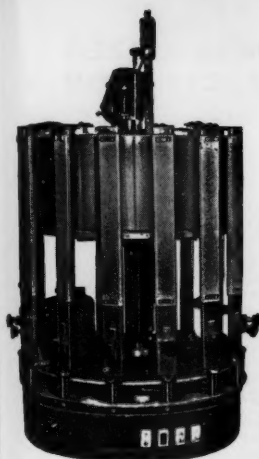
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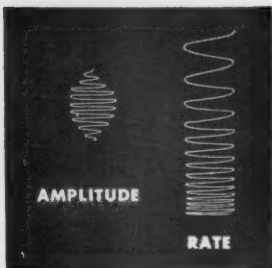


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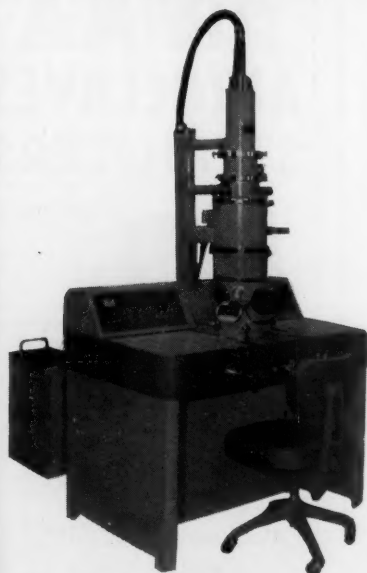
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Washington, D.C. (H. Welch, Div. of Antibiotics, Food and Drug Administration, Dept. of Health, Education, and Welfare, Washington 25.)

4-6. Design of Experiments in Army Research, 5th conf. (by invitation only), Fort Detrick, Frederick, Md. (F. G. Dressel, Office of Ordnance Research, Box CM, Duke Station, Durham, N.C.)

4-6. Eastern Analytical Symp., New York, N.Y. (P. Lublin, Publicity Chairman, Sylvania Research Laboratories, Bayside, N.Y.)

4-6. Industrial Management Soc., Chicago, Ill. (R. J. Mayer, IMS, 330 S. Wells St., Chicago 6.)

4-6. National Automatic Control Conf., Dallas, Tex. (G. L. Turin, Hughes Research Laboratories, Culver City, Calif.)

4-6. Society of Rheology, 30th anniversary, Bethlehem, Pa. (J. T. Bergen, Armstrong Cork Co., Lancaster, Pa.)

4-6. Technical Assoc. of the Pulp and Paper Industry, 13th alkaline pulping conf., Jacksonville, Fla. (TAPPI, 155 E. 44 St., New York 17.)

5-8. Group for the Advancement of Psychiatry, New York, N.Y. (American Psychiatric Assoc., 1700 18 St., NW, Washington 9.)

6. Gastroenterology Research Group, 9th semi-annual, Chicago, Ill. (E. Clinton Texter, Jr., Ward Memorial Bldg., Medical School, Northwestern Univ., 303 E. Chicago Ave., Chicago 11.)

8-13. International Rubber Conf., Washington, D.C. (B. S. Garvey, Jr., Pennsalt Chemical Corp., Industrial Chemicals Div., 813 Lancaster Pike, Wayne, Pa.)

9-11. American Petroleum Inst., 39th annual, Chicago, Ill. (API, 50 W. 50 St., New York 20.)

9-11. Association of Military Surgeons, 66th annual conv., Washington, D.C. (R. E. Bitner, AMS, Suite 718, 1726 Eye St., NW, Washington 6.)

9-11. Chemical Engineering, symp., Hamilton, Ontario, Canada. (Chemical Inst., 18 Rideau St., Ottawa 2, Ontario.)

9-11. Institute of Radio Engineers—Electronics Industries Assoc., fall, Syracuse, N.Y. (L. G. Cumming, IRE, 1 E. 79 St., New York 21.)

9-11. Instrumentation Conf., 4th, Atlanta, Ga. (W. B. Jones, Jr., School of Electrical Engineering, Georgia Inst. of Technology, Atlanta 13.)

9-12. Society of Exploration Geophysicists, 29th annual intern., Los Angeles, Calif. (B. Roberts, SEG, 1544 N. Highland Ave., Los Angeles 28.)

10-12. Electrical Techniques in Medicine and Biology, 12th annual conf., Philadelphia, Pa. (D. A. Holaday, College of Physicians and Surgeons, Columbia Univ., New York, 32.)

10-15. Laboratory Measurement and Automation Techniques in Chemistry, intern. cong., Basel, Switzerland. (ILMAC, 61 Clarastrasse, Basel, Switzerland.)

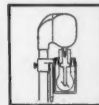
11-12. Clinical Anticancer Drug Research, Washington, D.C. (B. H. Morrison, III, Cancer Chemotherapy National Service Center, National Cancer Inst., Bethesda 14, Md.)

11-13. Gerontology Soc., Detroit, Mich. (R. W. Kleemeier, Dept. of Psychology, Washington Univ., St. Louis 5, Mo.)

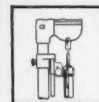
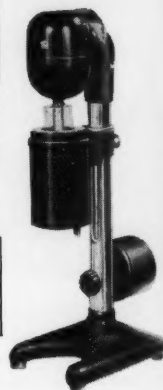
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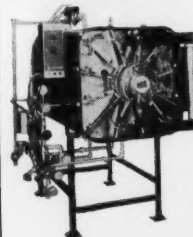
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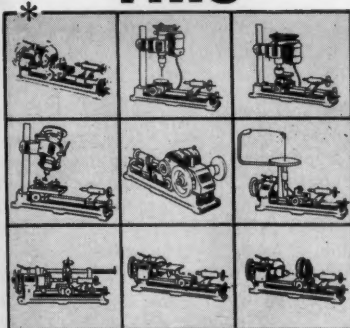
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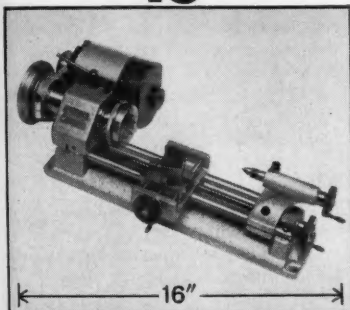
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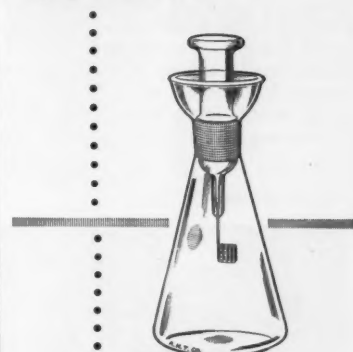
■ **BORANE DETECTOR** monitors airborne borane in concentrations less than 10 parts per billion. The detector cell contained in the instrument's sampling head consists of a pyridine-pyridinium chloride scrubber containing iodide and a small amount of iodine. Iodine is reduced to iodide by the boranes. When the iodine concentration drops to a preset level detected by amperometric electrodes regeneration is initiated by generating electrodes through a meter relay. The number of iodine-forming cycles in unit time is a function of borane concentration. Indication is provided either by a digital counter or by a potentiometer recorder. (Mine Safety Appliances Co., Dept. 40)

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■ **GAS AND VAPOR DETECTOR**, Kitagawa Unico model 400, consists of a hand pump and detector tubes for specific gases and vapors. The pump is designed to draw air samples at a reproducible fixed rate that duplicates flow conditions used in calibration. Reagents are adsorbed on fine-grain silica gel hermetically sealed in the glass detector tubes. Average error is said to be less than ± 5 percent at 68°F. Temperature correction tables are available. Thirty-six types of detectors are available for various gases in various concentration ranges. (Union Industrial Equipment Corp., Dept. 46)

■ **TIME-CODE GENERATOR** is an electronic clock supplying coded output signals. The base carrier signal is a 100 cy/sec sine wave from which interpolation to ± 0.0025 sec is said to be possible. Intervals of 0.2, 1, 10, and 60 sec are marked uniquely. Time announcements are made in decimal form every minute in 24-hour time. The instrument clock is a crystal oscillator stable to ± 3 in 10^7 /wk. Readout is an in-line, in-plane visual display. Start time may be preset to Greenwich Mean Time or other bases by a series of switches and may be

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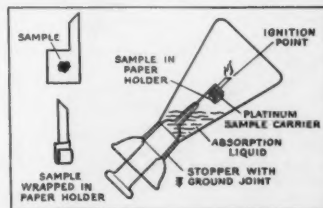
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See Wolfgang Schöniger, *Mikrochimica Acta*, 1956, Heft 1-6, pp. 869-876.

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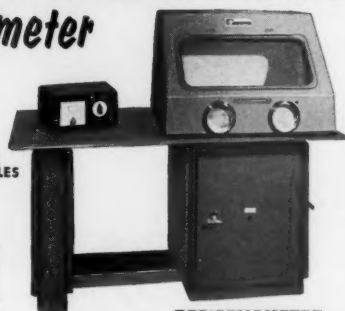
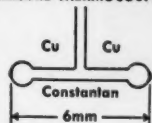
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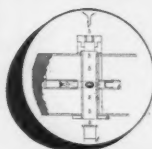
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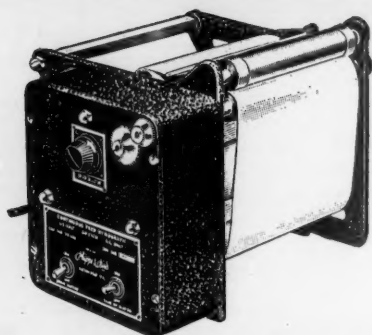
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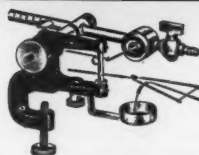


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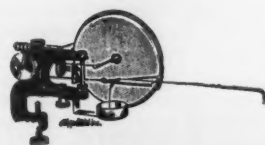
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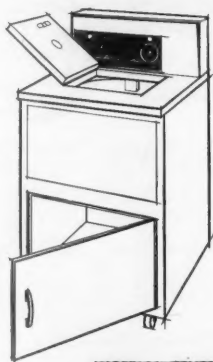
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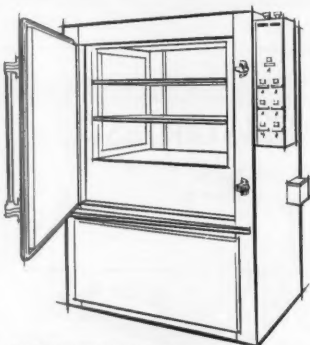
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■ **COUNT AND TIME SCALER** combines a decimal count scaler with an electronic time scaler. Preset time to 1000 sec, or preset count to 10^7 , is measured. Resolving time is 1 μ sec. The instrument includes a full-range discriminator fixed mercury pulse generator, and an electrically reset four-digit register. Positive or negative input is accepted. (Radiation Instrument Development Laboratory, Inc., Dept. 62)

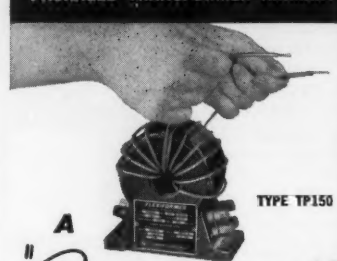
■ **VACUUM-TUBE VOLTMETER** measures voltage between 100 μ v and 1000 v, 1 mv full-scale, with accuracy ± 1 percent of full scale. Current is measured from 0.1 μ a to 1 amp with accuracy ± 2 percent of full scale. Resistance can be measured from 0.02 ohm to 5000 megohm. Voltage gain of the meter amplifier is 1000. Input is floating, with input resistance ranging from 10 megohm on the 1 mv range to 200 megohm on ranges above 100 v. The ohmmeter is a modified Kelvin bridge. (Hewlett-Packard Co., Dept. 58)

■ **OSCILLOGRAPH** is a two-channel, direct-writing recording milliammeter that uses electric or ink writing in rectilinear coordinates. Acoustic damping of the recorder movement is 50 percent of critical from current source drive. Source impedance for critical damping is 200 ohm. Constant-current response characteristic is flat from d-c to 60 cy/sec, falling off at the rate of 12 db/octave from 60 to 200 cy/sec. Current sensitivity is approximately 2.5 ma/mm. Linearity is 2 percent of 20 mm full-scale. (Cohu Electronics, Inc., Dept. 61)

■ **CONDUCTIVITY CELL** is designed for use at temperatures up to 200°C and pressures up to 300 lb/in.² (gage). Cell constant can be changed ± 10 percent, permitting calibration while the cell is at working temperature and pressure. A removable shield protects the electrodes from direct impingement of flowing liquid. Trapping of gas bubbles is prevented by design of the cell; the cell may be operated in any position. (Industrial Instruments, Inc., Dept. 60)

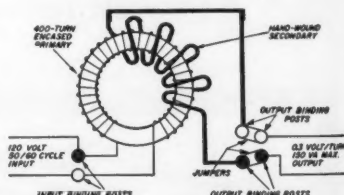
■ **MULTIPLIER PHOTOTUBE** is designed for high resolution in scintillation counting and nuclear-radiation spectrography. Transit-time differences under typical operating conditions are kept down to 0.3 μ sec. Width of the output pulse can

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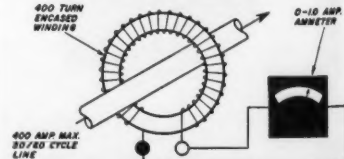
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be as little as 2 msec at half height with rise time of the same duration. Peak anode current is 1 amp, which is sufficient for direct use without amplification. At values up to 300 ma, anode current varies linearly with incident light flux. Fourteen multiplier stages provide gain of 10^8 or more, corresponding to an average cathode sensitivity of 50 $\mu\text{A}/\text{lu}$. Maximum useful diameter is 42 mm. Peak spectral response is $4200 \pm 300 \text{ \AA}$. (Mullard Ltd., Dept. 64)

■ **ULTRAVIOLET ANALYZER**, for automatic location of protein and nucleic-acid fractions eluted by column chromatography, monitors continuously during fraction collecting and records the ultraviolet absorbing qualities of each collection tube. Transfer from one sample tube to the next is indicated by a pip on the strip-chart record. The system is electrically stabilized by a servo-driven self-nulling circuit that balances out line and light fluctuations and compensates for baseline changes resulting from the solvents used. Optical densities as small as 0.03 are recorded. Cuvettes are optical quartz of capacity 1.1 ml. (Canal Industrial Corp., Dept. 65)

■ **DELAY LINES** of magnetostrictive design are said to have temperature coefficients of $5 \times 10^{-6}/^\circ\text{C}$ for fixed lines and for some adjustable models, and $25 \times 10^{-6}/^\circ\text{C}$ for other adjustable models. Delay stability ± 0.05 percent from -60° to $+90^\circ\text{C}$ can be provided. Output amplitude is constant over the entire operating range. (Deltone Inc., Dept. 66)

■ **SCANNING PRINTER** has 12-digit decoding and printing capacity for electronically controlled data from decimal or binary-coded decimal sources. A 12-column input keyboard provides for manual insertion of data. Input resistance of the data-input circuits is greater than 1 megohm, so that power drawn from data-originating circuits is small. (Clary Corporation, Dept. 68)

■ **SPEECH COMPRESSOR-EXPANDER** speeds speech to twice normal rate in nine steps or slows speech to one-third normal rate in nine steps while retaining intelligibility. Sensitivity for full-scale operation is 0.1 v r.m.s. Input signal recommended is 0.2 v r.m.s. Input impedance is 600 ohm. Frequency response is $\pm 2.0 \text{ db}$, 500 to 8000 cy/sec. Power supply is self-contained. (Kay Electric Co., Dept. 71)

■ **ANALOG-TO-DIGITAL RECORDER** records analog values of shaft rotation input in binary-decimal, punched-tape form. The tape accommodates 16 binary digits, equivalent to four decimal digits. The tape can be read directly or can be translated automatically into standard computer tape or punched cards. In addition,

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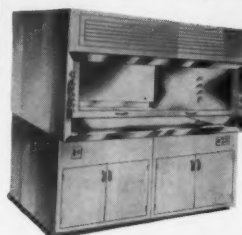
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tion to the punched-tape output, the device supplies digital information in the form of electrical contact closures that may be used for telemetering. (Fischer & Porter Co., Dept. 72)

■ **INDICATOR AND RECORDER** is a servo-operated device that provides digital read-out of electrical signals produced by transducers while simultaneously recording on a 3-in. strip chart. Chart drive is synchronous. Digital read-out accuracy is said to be ± 0.1 percent, chart accuracy ± 1 percent. (Gilmore Industries, Inc., Dept. 67)

■ **INERTIA SWITCH** is sensitive to acceleration axially, radially, or omnidirectionally from 0.01 to 500 g. Accuracy is said to be ± 0.1 percent, repeatability ± 0.003 percent. Automatic reset is optional with closure time variable, and adjustable acceleration setting can be provided. Weight is about 1 oz. (Safe Lighting, Inc., Dept. 73)

■ **SUB-AUDIO TUNED AMPLIFIER** is continuously adjustable from 0.3 to 3000 cy/sec. Attenuation of second harmonic is greater than 35 db, of third harmonic greater than 45 db, of higher harmonics,

50 db. Input impedance is 10 megohm shunted by 25 μ f. Output impedance is approximately 300 ohm. Amplification at the center frequency is approximately unity. (Electronics Lab., Inc., Dept. 74)

■ **ULTRAMICROTOME** produces automatically sections 75 to 400 Å for study with electron microscopes. Single sections 1 to 10 μ thick for optical microscopy can also be prepared. Specimen advance, actuated by thermal expansion of two nickel cores, is controlled by varying current through the coils surrounding the cores. Current is applied only during the return stroke of the mechanism. The effect of the current, in addition to heating, is to produce magnetostriction of the cores. The magnetostrictive contraction of the cores retracts the specimen so that it does not contact the knife on the return stroke. Cutting rate is approximately 30 sections per minute. (Philips Electronics, Inc., Dept. 84)

■ **OSCILLOGRAM AMPLITUDE TABULATOR** consists of a stationery unit, a printing counter, and a hand-held rectangular frame with two hairlines. One hairline is fixed; the other can be moved in either direction at fast or slow speed with a control knob. The instrument reads oscillogram and strip-chart amplitudes up to 6.5 in. and prints this information on adding-machine tape. A sequential count is recorded for each reading. Amplitude reading and timing count are directly visible on the counter. (Gerber Scientific Instrument Co., Dept. 76)

■ **POWER SUPPLY** for driving tape-recorder motors is available for operation from either 24 to 28 v d-c or 105 to 125 v, 48 to 62 cy/sec a-c. Output is 100 w with frequency regulation ± 0.02 percent. Third harmonic content is said to be negligible. (Precision Instrument Co., Dept. 80)

■ **MECHANICAL FORCE AMPLIFIER** is a mechanical servomechanism for amplification of small forces. Actuation requires less than 1 g; and output force can be as much as 500 g. The device uses a ring friction-driven by a roller. Input motion is applied to a control yoke that tilts the ring. The tilt causes the ring rotated by the roller to move laterally along the roller. Lateral motion of the ring is imparted to a follower which transmits the output force. Maximum force is developed at the null position. Time for full-scale travel of 2 in. depends on the angle of tilt and the rotational speed of the driver. At 300 rev/min the time ranges from 0.8 sec for 15-deg (max) tilt to 6.1 sec for 2-deg tilt. (American Meter Co., Dept. 81)

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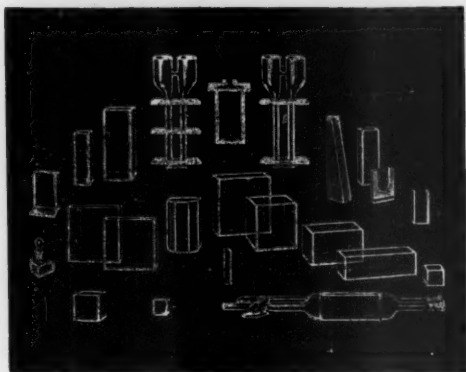
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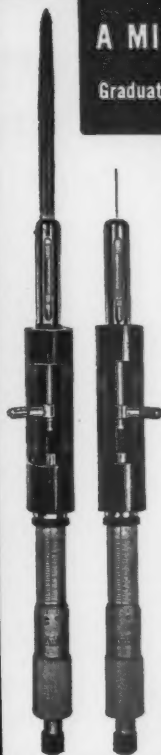


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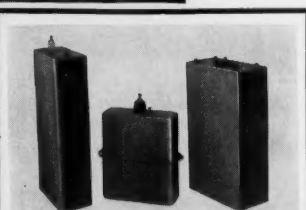
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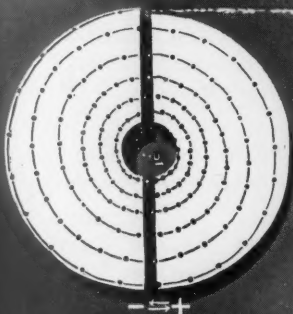
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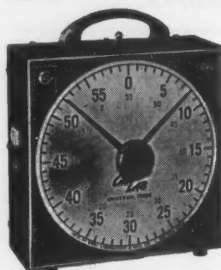
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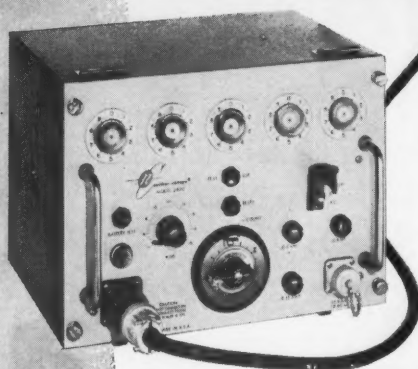
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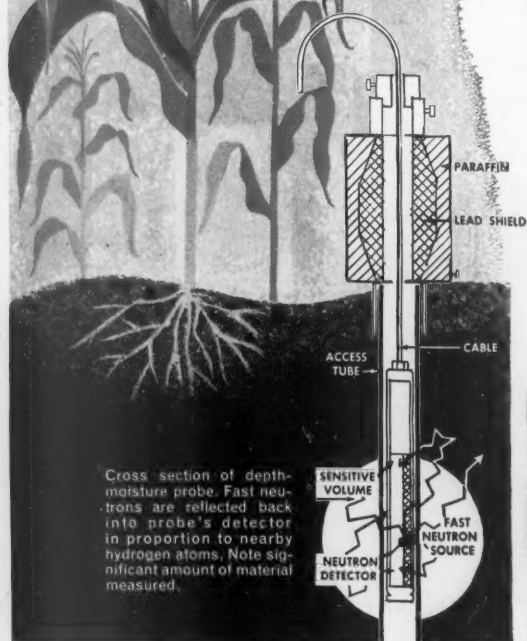
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